

Clinical aspects of compression therapy

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*aan mijn ouders
voor Margot, Olivier en Maartje*

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CHAPTER 1

VENOUS INSUFFICIENCY

BRIEF HISTORY OF VENOUS DISEASES

The process of walking upright of the homo sapiens, about 10 to 15 million years ago, had great impact on the lower limbs. The legs had to overcome the increased blood pressure due to the upright position. It became moreover a problem when people exercised less frequently, so that venous insufficiency could arise. Symptoms and treatment of venous diseases have already been mentioned in the Ancient times.¹ The Ebers papyrus was written in Ancient Egypt about 1500 BC. One section contains a description of "three types of lump", together with the advice that two types can be treated surgically but certain serpentine windings are not to be operated upon because that would be "head on the ground". Serpentine windings have been suggested to mean varicose veins and head on the ground a fatal bleeding. The first illustration of a varicose vein has been found on a votive tablet at the foot of the Acropolis in Athens (end 4th century BC.).

Praxagoras of Cos was probably the first physician to differentiate between arteries and veins when he stated that veins contained blood whereas arteries contained air. Galen of Pergamum (130-200 AD.) described for the first time the treatment of ulcers and varicose veins by venesection. He used silk ligatures and a blunt hook for tearing out varicose veins. The first description of bandages for the treatment of venous diseases is from Maitre Henri de Mondeville in the beginning of the 14th century. He correctly realized "avant la lettre" that compression bandages helped leg ulcers to heal because 'they would drive out the evil humours'. An important step forward in vascular medicine was the publication of *De Motu Cordis* by William Harvey in 1628. It was the foundation of our understanding of the blood circulation, and start of modern vascular medicine.

Richard Wiseman (1622-1676) invented a leather lace-up stocking for the treatment of venous disease of the lower limb, which was the forerunner of modern elastic compression stockings.

The year 1864 can be considered as the beginning of sclerotherapy. In his book, published in that year Chapman, reported that a Frenchman tried to sclerose varicose veins by injecting perchloride of iron.² Important early data of vein surgery are 1891, when Trendelenburg described the ligation of the long saphenous vein in the upper third of the thigh to prevent long saphenous reflux, and 1905 and 1906, when Keller and Mayo described techniques for 'stripping out' the long saphenous vein.³⁻⁵

Since that time many new inventions have been made and equipments have been designed to improve the cure and care of patients with varicose veins and venous insufficiency. Some of these will separately be discussed further in this chapter.

ANATOMY OF THE VEINS IN THE LOWER LEG

The venous system of the human lower limb leg can be divided into a superficial, perforating and deep venous system.⁶ The superficial and deep systems are divided by the fascia. The main superficial veins are the long (or great) and short (or small) saphenous vein.⁷ The

long saphenous vein emerges from the medial border of the foot, with a constant localisation anterior to the medial malleolus and running upwards along the medial side of the lower limb to the oval fossa, where it joins the common femoral vein (sapheno-femoral junction). The long saphenous vein has two constant tributary veins on the upper leg, called the anterior-lateral and posteromedial (semicircular) vein, and two on the lower leg, called the anterior and posterior arch (arcuate) vein.

The short saphenous vein emerges from the lateral side of the foot, running behind the lateral malleolus and upwards dorsally of the calf, joining the popliteal vein (parva-popliteal junction) at a variable level in the popliteal fossa. There are a number of variable connections between the long and short saphenous vein. All the other veins of the superficial system of the lower limb show a great variability between people.

Perforating veins connect the superficial system with the deep system. They are called perforating veins since they perforate the aponeurotic fascia, connecting the superficial and deep venous system. Beside these there are communicating veins, a term reserved for connecting veins in the superficial system.⁸ More than half of the perforating veins are accompanied by an artery.⁹ This is specially true for the clinically more important perforating veins. Perforating veins are numerous in number. Their average number varies from 64 to 155.^{10,11} Normally perforating veins are thinwalled and vary in diameter from 1 to 2 mm.¹² Many names have been given to the perforating veins with a more or less constant localization. Well known are the Dodd, Boyd and Cockett's perforating veins, all found on the medial aspect of the leg.

The three deep veins of the leg (anterior tibial, posterior tibial and peroneal vein) emerge from the foot and are usually paired, running as *venae comitantes* with the three crural arteries. The popliteal, femoral and profunda femoral veins are normally single veins. Although physicians do not display a major interest in the calf veins, the gastrocnemial veins and soleal veins are of importance for the venous circulation of the lower leg. Some even regard these veins as a separate venous system.¹³

A key structure of the peripheral veins is the venous valve, which under normal conditions prevents reflux of blood during walking. In quiet standing position they do not separate the blood column. Vein valves are normally bicuspid. A properly functioning valve can withstand the hydrostatic pressure in the standing position plus an overload imposed on by straining. Normal valves can withstand a remarkable high retrograde pressure of more than 300 mmHg.¹⁴ Valves are found in veins of more than 1 mm diameter. The number of venous valves has been found to be less in varicose veins than in normal veins. There is no difference between man and woman. Also aging does not appear to produce a decrease in venous valves, although a decrease of 19% was found by others.¹⁵ The smallest veins containing valves lie at the dermal subcutaneous junctions and are extremely variable.¹⁶

The microcirculation of the skin of the lower leg is much more complicated in its anatomy and function than the macrocirculatory structures. The arterioles and venules form two important plexuses in the skin: an upper horizontal network in the papillary dermis from

which the capillary loops of the dermal papillae arise and a lower horizontal plexus at the dermal-subcutaneous interface.¹⁷ The lower plexus has connection via perforating vessels with the deep system. The microcirculatory bed has traditionally been divided into arterioles, capillaries and venules. Furthermore precapillary sphincters and postcapillary venules can be distinguished.

PHYSIOLOGY AND PATHOPHYSIOLOGY

In supine position the venous pressure in the foot is between 10 and 15 mmHg.¹⁸ In this position there is only a small difference in pressure between the leg and the right atrium of the heart. In standing position the venous pressure at the ankle region is equal to a column of blood from the heart to the ankle. The pressure at the ankle is thus dependent on the height of the subject. In general, the venous pressure at the ankle in standing position is between 90 and 110 mmHg.^{19,20} Of course this is only true if all the valves are open, which the venous valves normally are when standing quietly. The pressure, measured in this position, is called the standing venous pressure (SVP). This SVP is only dependent of the length of the individual person.

Four different forces take care of returning the blood to the chest and the heart. Minor forces are the *vis à fronte* (negative chest pressure) and the venous tone. This venous tone is provided by an interaction between the smooth muscles of the tunica media and the elastic properties of the vein wall. Changes in tone are mediated through the sympathetic nerves and by circulating smooth muscle stimulants. The venous tone in the subcutaneous veins is affected by emotion, pain, sleep, exercise, core temperature and position.²¹ The most important reflex role is thermoregulation.

The *vis à tergo* (pressure difference between venules and heart) is a more important force than often thought of. It keeps up the flow of blood in the veins in for example the quiet standing position. This flow is relatively slow and can therefore not be detected by for example Doppler ultrasonography or Duplex scanning. The fourth force, the venous muscle pump, is by far the most important one. During walking, contractions of the calf muscles will generate high pressures in the deep veins. This will squeeze the blood back to the thigh. The venous valves prevent reflux from proximal to distal and from the deep to the superficial venous system. This is the case during walking activity as well as after ending the movement. This interaction between valves and muscles is known as the muscle pump activity. Beside the calf muscle pump, there also exists a foot and thigh muscle pump.

The calf muscle pump mechanism plays a critical role in the reduction of the venous pressure at the ankle. As soon as a subject starts to walk, the muscles in the calves will pump the blood up toward the chest. The pressure at the ankle will decrease to about 10 mmHg.²²⁻²⁵ It is called the walking venous pressure (WVP). If the subject stops walking the pressure will again increase to the original standing venous pressure of about 90 mmHg [see Figure 1].

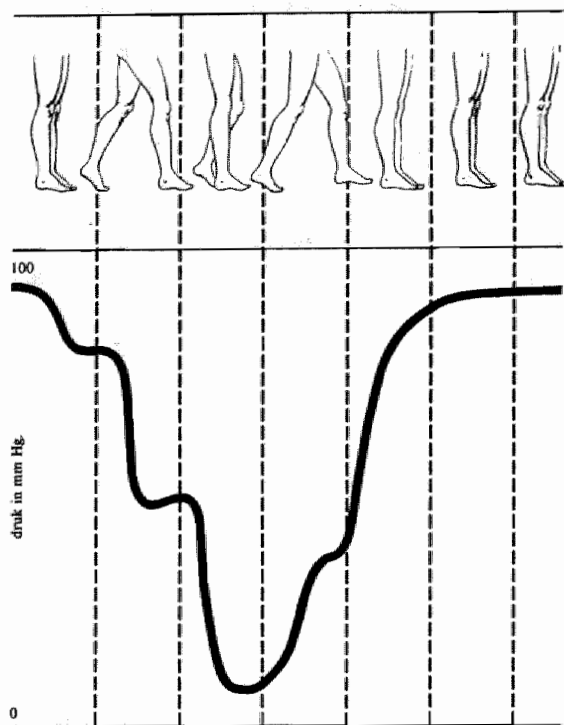


Figure 1. Venous pressure values in upright and quiet standing position and after having walked several steps.

The time to return to the original standing pressure is called the venous refilling time (VRT). This is of course only true if the arterial influx remains constant.

The pressure in the capillaries is in normal condition about 15 mmHg higher than the pressure in the veins. It will follow the venous pressure during the walking activity. This means that in (quiet) standing position the transmural pressure (intra-capillary pressure minus interstitial pressure) is about 105 mmHg, if the interstitial pressure is accepted as being zero. This pressure will influence the filtration and diffusion equilibrium of the tissue. If this pressure increases oedema can occur. After active muscle movements the venous as well as the transmural pressure will decrease and the oedema will be reduced.²⁶

Damage or incompetence of the venous valves and subsequently reflux in the superficial, deep or perforating system (or a combination of the three) is the most important reason for venous insufficiency. The venous valve dysfunction can be due to primary varicosity, a past history of deep venous thrombosis and/or insufficient perforating veins. Venous reflux leads to an insufficient pump function of the calf muscles and an increase of the walking venous

pressure at the ankle. This is called continuous high ambulatory venous pressure or a venous hypertension. This increased venous pressure will in time induce dilatation and a tortuous appearance of the capillaries. As a result of the latter, the transmural pressure is constantly high and capillary filtration increases, leading to capillary leakage and oedema formation. From this point on functional changes of the microcirculation induce a lot of pathological alterations, leading to the syndrome known as chronic venous insufficiency (CVI).²⁷ Gradually the clinical signs of CVI will become more evident. So, CVI can be defined as a combination of an altered venous circulation, a continuous elevated intravenous pressure (due to the upright position) and consequently the development of skin abnormalities such as leg ulceration. Other, more rare reasons for CVI are angiodysplasias with arteriovenous shunts, local compression of venous vessels, prolidase deficiency and Klinefelter's syndrome.²⁸

In the course of this disease several changes of the skin can be detected, such as erythema (confluencing stasis spots), corona phlebectatica (ankle-flare), pigmentation and white atrophy (of Milian).²⁹ In long standing cases, brownish colored, indurated patches, which are nowadays mostly described as lipodermatosclerosis, will occur. Finally, the end stage of the disease is ulceration. One of the earliest classifications of chronic venous insufficiency has been designed by Widmer [see Table 1].³⁰ The Widmer classification is mainly based on clinical symptoms and is still the most widely used because of its simplicity. This is how-

Table 1. *Widmer classification.*

Class	Symptom
I	Corona phlebectatica
	Oedema (subclinical)
II	Oedema
	Pigmentations
	Lipodermatosclerosis
	White atrophy
III	Leg ulcer
	Leg ulcer in the past

ever also the disadvantage of the Widmer classification because it is typically for CVI to aggravate in time. This means automatically that the clinical lesions are not always correlated with the severity of the disturbances of the venous system. This is another reason why the classical clinical classification according to Widmer is only partly helpful in classifying CVI. It is better to use a true haemodynamic parameter such as the venous refill time or the walking venous pressure. However the clinical manifestations are helpful of classifying CVI and are therefore still of great value in daily practice.

Recently a new, more thorough classification called the CEAP (or Hawaii) classification has been designed [see Table 2].³¹ It tries to categorize patients with venous diseases on the basis of different parameters: Clinical (skin symptoms and complaints), Etiological (primary, secondary and congenital), Anatomical (superficial, perforating or deep) and

Tabel 2. CEAP-classification developed by the American Venous Forum and North American Society of Phlebology in cooperation with the diverse European societies on phlebology.

Clinical classification	
class 0	: no visible or palpable signs of venous disease
class 1	: telangiectases or reticular veins
class 2	: varicose veins
class 3	: oedema
class 4	: skin changes ascribed to venous disease
class 5	: skin changes as defined above with healed ulceration
class 6	: skin changes as defined above without healed ulceration
Etiological classification	
Congenital	
Primary - with undetermined cause	
Secondary:	
	- post-thrombotic
	- post-traumatic
	- other
Anatomical classification	
<i>Superficial veins</i>	
1	Teleangiectases/reticular veins
	Long saphenous
2	Above knee
3	Below knee
4	Short saphenous
5	Non-saphenous
<i>Deep veins</i>	
6	Inferior Vena Cava
	Iliac
7	Common
8	Internal
9	External
10	Pelvic
11	Common
12	Deep
13	Superficial
14	Popliteal
15	Crural - anterior tibial, posterior tibial, peroneal
16	Muscular - gastrocnemial, soleus, other
<i>Perforating veins</i>	
17	Thigh
18	Calf
Pathophysiological classification	
Reflux	
Obstruction	

Pathological (obstruction, reflux). Again a major disadvantage of this classification is that the staging may change in time. For instance a patient with a venous leg ulcer will be classified differently once his ulcers have been healed, although his venous haemodynamic disturbances are still the same.

HYPOTHESES CONCERNING THE SYMPTOMS IN CVI.

Skin alterations which occur in the course of CVI are directly related to the dysfunction of the venous system and microcirculation. During the last decade more details have been elucidated on the relationship between the macro- and microcirculation. The continuous high venous pressure during standing and walking is transmitted to the micro-vascular system of the skin, leading to dilatation, enlargement, tortuosity and formation of glomerulus-like capillaries.³² The interendothelial spaces enlarge and an abnormal high capillary filtration rate induces an accumulation of initially water, ions and salts, and later also other larger plasma components into the interstitium.^{33,34} In a later stage also red blood cells will extravasate. Skin biopsies of venous insufficiency lesions furthermore show an apparent proliferation of capillaries and a so-called peri-capillary halo. The total number of capillaries is reduced, although in histological sections the tortuous loops might give the impression of a capillary increase. The exact pathophysiologic pathway of the development of lipodermatosclerosis, white atrophy and venous leg ulceration is however still unsolved.

Several hypotheses have been postulated in the last decades to explain the underlying mechanism [see Table 3]. The earliest hypothesis on stasis of blood was posited in 1917 by Homans.³⁵ He suggested that due to stasis of blood at the ankle, the oxygen content of the blood would drop and causes ulceration. In later studies the oxygen content appeared however to be elevated.³⁶ Another theory from 1953 deals with arteriovenous shunting.^{37,38} This theory has also been put aside although there is no good evidence against it.

Table 3. *Hypotheses on the pathophysiology of venous leg ulceration and skin symptoms like lipodermatosclerosis.*

Author	Year	Hypothesis
Homans	1917	Venous stasis
Piulachs	1953	Arteriovenous shunting
Browse/Burnand	1982	Fibrin cuffs
Bollinger	1982	Microthrombi
Coleridge Smith	1988	White cell trapping
Falanga	1992	Growth factor trapping

Browse and co-workers from the St. Thomas Hospital in London postulated a theory known as the "fibrin-cuff theory".³⁹ They stated that there is leakage of fibrinogen from the capillaries. This induces the formation of a fibrin-cuff around the capillaries, leading to a diffusion barrier for oxygen and nutrients and finally to tissue hypoxia and ulceration.^{40,41} Recently doubt has risen on the fibrin cuff theory. Michel made it acceptable that in CVI fibrin cannot act as a diffusion barrier.⁴² Out of the group of Neumann fibrin cuffs have been proven to be found in only 73% of the cases of dermato- et liposclerosis and that $TcPO_2$

values do not differ significantly between fibrin positive and negative patients.⁴³ Furthermore, they stated that in several other conditions like wound healing, chronic inflammation and porphyria cutanea tarda, fibrin deposits are also present.⁴⁴

By using capillary microscopy Bollinger et al. were also able to make it acceptable that there is a normal or reduced number of capillaries in lipodermatosclerotic skin.⁴⁵⁻⁴⁷ They could furthermore demonstrate that in severe cases of CVI with white atrophy, microthrombosis occurs and that this process is responsible for the decrease of the capillary density in this particular skin lesion. Also in histological sections of dermato- et liposclerotic skin lesions these microthromboses can be found.⁴⁸ It is nowadays known as the "microthromboses theory".

In 1988 attention has been asked for the observation that in legs of patients with CVI white cells are accumulated when compared to legs of healthy persons.^{49,50} This "White cell trapping" is thought to play a role in the development of venous ulceration and other skin symptoms.⁵¹ In this hypothesis white cells will, due to the venous hypertension, adhere ("trap") to the endothelium of the capillaries. This induces a release of proteolytic enzymes and superoxide metabolites causing destruction of the tissue. "White cell trapping" may occur because of alterations in the blood flow, in the blood itself, in the white cells or in the endothelial cells such as alterations of adhesion of white cells to them. The nature of active leucocyte adherence is not fully understood, however adherence proteins do play an important role.⁵² Some of these adhesion molecules are: intercellular adhesion molecule-1 (ICAM-1), endothelial leucocyte adhesion molecule (ELAM-1) and vascular cell adhesion molecule (VCAM-1). Veraart et al. have performed a study with a panel of these monoclonal antibodies on tissue from the ulcer border. They found a moderate to strong expression of ELAM-1 underneath venous leg ulcers, although not beside the ulcers. There appears to be no up-regulation (enhanced surface expression as measured by monoclonal antibodies) of ICAM-1, and a total absence of VCAM-1 along the border area of the ulcer.⁵³ The results assume a disturbed attraction of granulocytes to the ulcer tissue causing delayed healing. Other experiments on the expression of ICAM-1 and ELAM-1 in lipodermatosclerotic skin and healthy control skin showed no significant difference.^{54,55}

Up to now there are no animal models available to study venous insufficiency and the pathophysiology of venous skin alteration and leg ulcers. It could be demonstrated in the limbs of animals that there is an increase in capillaries after several weeks when the femoral artery is connected with the femoral vein, thus creating a venous hypertension.⁵⁶ These animals however never developed a (venous) leg ulcer. Recently Veraart et al. were able to observe patients with Klinefelter's syndrome (XXY) complicated by skin changes and leg ulceration clinically indistinguishable from the lesions seen in chronic venous insufficiency, but without objective valve disturbances of the venous circulation.^{57,58} This patient group can lead to new keys in understanding the complex pathomechanisms behind venous diseases. We observed in our group of patients with Klinefelter's syndrome obvious disturbances in the fibrinolysis as measured by an elevated plasma activity of plasminogen activator inhibitor 1 (PAI-1) only partially decreasing upon venous occlusion. Patients with venous leg ulcers

have shown to have normal activity of PAI-1.⁵⁹ Increased levels of PAI-1 can be regarded as a sign of a diminished fibrinolysis in Klinefelter's syndrome which might contribute to microthrombi, tissue hypoxia and cell necrosis.

CLINICAL SYMPTOMS OF CHRONIC VENOUS INSUFFICIENCY

In the course of chronic venous insufficiency a great variety of skin lesions will develop. All these skin abnormalities are due to changes in the venous macrocirculation and secondary changes of the microcirculation. How many patients with varicose veins and/or insufficiency of the perforating and deep venous system will develop skin symptoms has never been investigated properly. The data differ from 17-50%.^{60,61} In most patients there is no specific time interval between the occurrence of venous insufficiency and specific skin symptoms.

Oedema, this is often the first sign of a decompensating venous system. For example, an isolated insufficient perforating vein can produce mild oedema around the ankle. Oedema is mostly more profound at the end of the day and resolves during the night. Patients usually complain of a feeling of heaviness and tiredness of their legs and occasionally night cramps. Due to the continuous venous hypertension transmitted to the capillaries, the capillary filtration rate increases. This causes a disturbance of the normal diffusion/filtration balance of the endothelial wall. Oedema in venous insufficiency is typically pitting oedema, mainly concentrated around the ankles. This is in contrast to lymphoedema which is in later stages non-pitting and mainly concentrated at the toes and forefoot. In long standing venous insufficiency the lymphatic system will become overloaded due to the failing venous system. This will at the end lead to decompensation of also the lymphatics and so to secondary lymphoedema.⁶² Only in long existing CVI the "dermal back flow" develops into true visible lymphoedema.

Pressure erythema (stasis spots) which at a closer look is not a true erythema, but consists of confluated very thin red teleangiectasias, is the result of the high capillary pressure. It is already visible in early stages of CVI.

Pigmentations develop also at an early stage of CVI. In the beginning, small points, slowly confluating to macular erythematous to brown eruptions can be found, especially around the region of the medial malleolus. They are often described as "dermite jaune d'ocre". The pigment is recognized as iron and not as melanin. Iron deposits are the result of extravasation of erythrocytes.⁶³ During the breakdown process of the erythrocytes, the iron is phagocytosed and the siderophages remain present in the pars papillare of the dermis. If the process leading to CVI continues, the pigmentation becomes more visible and finally dark pigment is seen in the so-called dermato- et liposclerotic plaques. Only in cases of inflammation some melanin deposits are seen and histologically recognized as post inflammatory pigmentation. After elimination of the inflammation, this kind of pigmentation will fade away in time.

Dermato- et liposclerosis is a specific skin complication of CVI and has been given many names in the past (see Table 4).⁶⁴ The term is reserved for the hyperpigmented, indurated and sclerotic eruption seen in patients with most often long standing CVI. The skin symptoms are usually restricted to the medial side of the lower leg. The condition has an acute, inflammatory phase and

a chronic, fibrotic stage, although a spectrum exist.⁶⁵ In the acute phase *dermato- et liposclerosis* occurs with erythema, scaling and induration. The eruption is then normally warm and tender. The late phase is the more typical indurated sharply demarcated pigmented and atrophic skin.

Table 4. Synonyms for *lipodermatosclerosis*

Hypodermis sclerodermiformis	Huriez	1955
Dermatosclérose	Pérard / Kint	1960
Sclérose dermohypodermique	Vigoni	1965
Hypodermite veino-lymphatique	Chatard	1974
Liposclerosis	Browse	1979
Venous lipodermatosclerosis	Burnand	1980
Hypodermite lympho-veineuse	Bertrand	1981
Hypodermite veineuse en plaque	van der Stricht	1988
Sclerosing panniculitis	Jorizzo	1991
Dermato- et liposclerosis	Blaauw / Neumann	1993

The most characteristic histological findings are dermal and subcutaneous fibrosis as well as vascular changes. The rarefaction and dilatation of the capillaries are most conspicuous. The fibrotic changes of the dermis can be compared with systemic sclerosis. There is an extensive extravasation of erythrocytes which have been phagocytosed. A lot of iron will be found in the specimens. In the acute phase an inflammatory process is present, mainly consisting of lymphocytes and macrophages. This reactive inflammation will in time show the same characteristics of granulation tissue. In time a bradytrophic, fibrous scar tissue is built up leading to the sclerosis. The most advanced cases show pronounced sclerosis within the dermal fat with a diminished or absent inflammatory cell infiltrate. *Dermato- et liposclerosis* is a skin eruption that is highly at risk for the development of a venous leg ulcer.

White atrophy (*atrophie blanche*, livedoid vasculitis, capillaritis alba) was first described by Milian in 1929, who supposed a syphilitic etiology, an opinion which has been incorrect. It consists of a white patchy ivory-tinged or porcelain-coloured, irregular shaped, skin with only a few visible red capillaries.⁶⁶ There is some hyperpigmentation in the border. It is in most cases a late symptom of CVI. However, white atrophy can be found in a variety of other diseases. The capillaries are much greater in diameter, often up to 50 micrometer (normal about 10 μ m). Histological sections the skin of white atrophy show a thin and atrophic epidermis and a sclerotic dermis with a lot of fibrosis. Some of the (giant) capillaries show characteristic hyalinthrombi and slugged red blood cells in vessels of the reticular dermis. There are surprisingly few signs of inflammation. Occluded capillaries have also been demonstrated with fluorescence capillary microscopy by Bollinger and co-workers. Also TcPO₂ measurements were shown to be extremely low. So, ulceration can easily develop in white atrophy eruptions and is often extremely painful. They also have a reputation for a bad

healing tendency. It is still not clear whether the atrophy should be regarded as sequelae or rather as a prerequisite for ulceration.

Venous ulceration is the end stage of CVI. The break down of the skin can be spontaneous or after minimal trauma. Most leg ulcers (about 88%) occur at the gaiter area and mostly at the medial site.⁶⁷ This is the place of the lower leg where the influence of gravity is largest, the skin is drained by the (often incompetent) long saphenous system and (incompetent) perforating veins are present. Venous leg ulceration is a common problem with a great morbidity. The base of the ulcer is mostly covered with a thick granulation tissue, and the edges are sharp and cyanotic. The area around a venous leg ulcer can be macerated, eczematous and pigmented. Many patients (about 60%) with a venous ulceration are at risk to develop a contact sensitization, mainly against parts of topically applied medical creames and ointments.⁶⁸ Most common are vehicle constituents, antibiotics and the so-called 'paragroup'.

EPIDEMIOLOGY OF VENOUS DISEASES

Epidemiological data of venous diseases leave many questions behind. The literature on epidemiology of venous diseases, especially varicose veins, is inadequate. In a recent critical review of the literature identified from computerized database (1985-1994), Beaglehole encountered only one study which met the minimal criteria for high quality, in that randomly chosen community samples were studied by direct examination and explicit criteria for varicose veins were used.^{69,70}

Varicose veins have a prevalence varying from 15 to 50% of the total adult population depending on the definition and type of study.⁷¹⁻⁷³ According to the figures of the continuous morbidity registration of general practitioners (CMR) in the Netherlands the incidence of varicose veins in the general practice is 10 new cases in 1.000 women per year and 3 new cases in men.⁷⁴ There is a strong increase in incidence with age; 8% of women between the age of 20 and 29, increasing to 41% in the fifth, and 72% in the seventh decade of life.⁷⁵ A similar rate of increase in the incidence of varicose veins occurs in men.⁷⁶ Most studies show a higher prevalence in women; 79% of the consultations because of varicose veins in the Netherlands concerned women. Only Widmer found in his famous Basel study a higher prevalence in men, but he investigated a factory population which probably was a selected group of patients. Varicosity in childhood is rare, occurring almost exclusively in association with congenital vascular malformations such as Klippel-Trenaunay, Frederik Parkes-Weber, and Bockenheimer syndrome.

It has been estimated that CVI will develop in almost 50% of patients with major varicose veins.⁷⁷ The same was found in the Basler study by Widmer. CVI complicated by ulceration has been the item of many studies in the past.⁷⁸ One should remember that many of these studies evaluated all leg ulcers within a population and not only venous ulcers. Furthermore many studies used questionnaires. The largest and certainly the most thorough study has

been performed by Callam.⁷⁹ The overall prevalence of current ulceration in the adult population was 1.5 per 1000. In women over 80 years it was 20 per 1000. Recent studies from Sweden and Australia showed much higher figures.⁸⁰⁻⁸² For example, the point prevalence of leg ulcers for the adult population was calculated for Sweden at 0.6%, but only half of the patients were known to healthcare providers. So the real prevalence will be somewhere around 1.2%. Many ulcer 'patients' probably never visit a doctor! This means that CVI is a major but often underestimated problem, with a lot of discomfort for the patient and high costs for the society.^{83,84} For example, the total costs for varicose veins and related diseases in 1992 in West Germany has been calculated at 953 million German marks.⁸⁵

DIAGNOSIS OF VENOUS DISEASE OF THE LOWER LEG

The evaluation of venous disease is important, though often confusing. Many patients still receive treatment without a proper investigation and consequently diagnosis. First the history should include the varicose complaints as heaviness, cramps, oedema formation, pain and numbness. A past history of deep vein thrombosis or thrombophlebitis should be searched for. Also previous treatments of the veins should be noted. Further important factors in venous patients, especially in patients with a leg ulceration, are arterial disease, diabetes mellitus, cardiac failure, low albumin, use of steroids and also lupus erythematosus or other systemic diseases.

Clinical examination with the classical Trendelenburg and Perthes tourniquets tests are misleading and do not have a proper sensitivity and specificity. Furthermore they provide little information about the state of the deep veins. Subsequent investigations to elucidate the underlying abnormalities (obstruction and/or reflux) in the venous system and to determine their severity by quantitative measurements are therefore mandatory in most patients.⁸⁶ Nowadays it is possible to investigate each patient with a wide scala of tools. These investigative techniques can be divided in 1) anatomical- (phlebography and duplex) and 2) functional (Doppler ultrasound, duplex, plethysmography) investigation. The techniques are either invasive or non-invasive. It is up to the physician to choose the most adequate technique before starting the treatment. In this chapter the most widely used methods to investigate venous disease will be discussed. The first two provide mainly anatomical information. The other 5 evaluate the functional status of the venous system.

Phlebography

Berberich and Hirsch published the first description of phlebography in 1923.⁸⁷ In the beginning the ionic contrast media used were hyperosmolar, compared with blood and tissue fluid, causing many side effects. The newer generations of contrast media are however less irritating to the endothelium, better tolerated by the patients and therefore a great step forwards. Although the technique is invasive, phlebography is still valuable in the management of a lot of patients with venous diseases.⁸⁸ Different methods of phlebography are available, each demonstrating a particular clinical problem. It is, for example, possible to assess the

anatomy of the venous system of the leg by the standard ascending phlebography. With descending phlebography one can demonstrate saphenofemoral reflux and deep valve incompetence. Varicography can be used to study complicated varicosities. Also dynamic phlebography can be used with the aid of a video during the investigation.

Duplex scanning

Duplex scanning allows the examiner to visualize the venous system in real time B-mode imaging combined with Doppler ultrasound. Color flow imaging is even newer and provides instant visualization of blood flow and its direction. First Duplex scanning was used for the diagnosis of deep venous thrombosis.^{89,90} Now the overall sensitivity and specificity of duplex scanning in the diagnosis of deep venous thrombosis is more than 90%.⁹¹

At the end of the eighties its use has been extended to study venous valve function, localization of perforating veins and detection venous reflux. It has been demonstrated that there is a correlation between the sum of reflux from all the veins and the occurrence of skin symptoms in CVI.⁹² Also quantitative segmental evaluation of venous valve reflux has been possible with duplex scanning ultrasound.⁹³

Being non invasive, duplex scanning is the ideal method for the evaluation of venous diseases and almost universal accepted.⁹⁴ The technique is however time consuming and highly dependent on the investigator's skill.

Doppler Ultrasound

The first vascular application of Doppler ultrasound dates back to 1960 when Satomura and Kaneko described a method of studying changes in blood flow in peripheral arteries using an ultrasonic blood rheograph.⁹⁵ Later the technique was widely advocated for arterial as well as for venous disease.⁹⁶ The instrument is based on the principle of the Doppler effect and consists of an ultrasound emitting crystal and a receiving crystal. Sound waves are directed into the tissue and reflected off the blood cells traveling through the vessel being examined. Continuous wave Doppler ultrasound equipment is adequate for venous examination, even though the signal represents a composite of the flow in all vessels in the path of the ultrasound beam. Pulsed Doppler ultrasound is used when the intent is to focus the beam at a particular depth.

At this moment Doppler ultrasound is probably the simplest, most rapid and most widely used technique to evaluate patients with varicose veins and CVI. The positive predictive value of Doppler examination is superior to the physical examination.⁹⁷ Also the negative predictive value is reasonably good. Doppler ultrasound equipment is easily commercially available, cheap and simple to handle. It is advisable for the superficial and perforating venous system to investigate a venous patient in standing position. By compressing the limb distal to the Doppler probe, one increases the flow through the vein, and an immediate increase in the signal intensity should be heard, using a bidirectional system. After releasing the compression there should be no flow signal. Longer lasting flow signals on release are an indication for reflux and insufficiency or destruction of the venous valves. In the same way the deep venous system can be evaluated with a 5 MHz probe (femoral, popliteal and

posterior tibial veins), but now in supine position. Also perforating veins can be searched for with the aid of tourniquets. The accuracy of the technique increases with the experience of the investigator.

Photoplethysmography / Light-reflex rheography

Photoplethysmography (PPG) is a non-invasive optical technique for measuring tissue blood perfusion. It was Hertzman who in 1938 for the first time described a photoelectric plethysmographic method for measuring skin circulation by relating the intensity of the light reflection of the skin to its blood content.⁹⁸ Several PPG methods have since then been described and tested for their practical use. The most important parameter for practical use is the venous refilling time (VRT) after finishing a standardized exercise of the calf muscles. This VRT has been shown to be good reproducible, and to correlate well with the foot vein pressure recovery time.^{99,100} Despite this, the technique has not been accepted by all physicians.¹⁰¹⁻¹⁰³

Light reflection rheography (LRR) is a technique based on the principle of PPG. The technique was developed by Wienert and Blazek in the early 1980's.¹⁰⁴ The probe contains three light-emitting diodes instead of one in PPG. Advantages are that a greater part of the superior dermal plexus is being measured, and that the LRR is less influenced by surrounding light. LRR has been used in recent years as a routine screening test in the assessment of patients with varicosity or CVI.¹⁰⁵ In his study van Walsum demonstrated that the venous refilling parameter measured by LRR has a high (97%) positive predictive value in the pre-operative diagnosis of long saphenous vein insufficiency. The negative predictive value was however shown to be much lower.

Digital photoplethysmography (D-PPG) is a further optoelectronic development of LRR.¹⁰⁶ This second generation LRR adjusts the emitted light until a predetermined signal level of the reflected light is obtained, thus compensating for the different conditions of cutaneous optical density. The instrument has a good correlation with the previously mentioned LRR.¹⁰⁷ It is smaller in size (pocket size) and therefore more practical in use.

Strain gauge-plethysmography

The strain gauge plethysmograph (SGP) consists of a silastic tube filled with mercury positioned in an electric circuit. It is placed around the limb with just enough stretch to ensure good contact. When the volume and circumference of the limb increases, the length of the strain gauge is also increased by a corresponding amount. The electrical resistance of the gauge varies with its length, and hence variations in the measured voltage across the gauge will reflect changes in the limb circumference. Assuming the limb is cylindrical, it could be demonstrated by Withney et al. that the relative change in the volume of a segment is equivalent to twice the relative change in its circumference.¹⁰⁸ SGP was initially used to assess the arterial circulation. Later it was used in the diagnosis of deep vein thrombosis measuring the maximum venous outflow after occlusion, an application now taken over by Doppler ultrasound and duplex techniques. Nowadays new tests have been developed for the strain gauge method, such as the measurement of (deep) venous resistance and the supine venous pump function test according to van Gerwen.¹⁰⁹

Air-plethysmography

Air plethysmography (APG) has already been used in the early 1960's to study relative volume changes of the leg in response to postural changes. It was reintroduced by Nicolaides and his co-workers for venous diagnosis in 1986.¹¹⁰ The main advantage is that it is now possible to calibrate the system. With the instrument volume changes of the whole lower leg (in milliliters) can be measured instead of volume changes of a segment as measured with SGP. A 36 centimeters long tubular polyurethane air-chamber is placed around the lower leg covering from knee to ankle. This tube is inflated with air to 6 mmHg and connected to a calibration syringe and pressure transducer and computer with a special designed software. By inflating 100 ml of air into the chamber a pressure-change is registered and the system is calibrated.

In a normal procedure first the maximal venous outflow is measured to detect (deep) venous obstruction. This is measured in lying position. Then a venous filling index (90 percent of the venous volume measured at the leg after changing from supine to standing position) can be assessed. This parameter has been well correlated with the severity of venous diseases and specially skin changes as lipodermatosclerosis and leg ulceration.¹¹¹ Furthermore the effect of vein surgery can be evaluated.¹¹²

Ambulatory venous pressure

Measurement of foot vein pressure is well established as reference method for the overall evaluation of the venous calf pump function of the lower limb. The pressure in a dorsal foot vein is measured in standing position and after performing standard exercises. If the pressure does not decrease sufficient after exercise the subject has an 'ambulatory venous hypertension'. The test is highly reproducible and shows a high positive correlation with the incidence of venous ulceration. The test is still accepted as the gold standard of the venous calf pump function assessment. All new noninvasive tests should be validated with it. However, because the measurement is invasive, it cannot be repeated frequently nor can it be used as a screening test.

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CHAPTER 2

REVIEW OF COMPRESSION THERAPY

INTRODUCTION

Compression therapy is a well known form of treatment in phlebology. It has been described and practiced for many centuries.^{1,2} Hippocrates (460-377 B.C.) was probably the first who associated varicose veins with leg ulcers and suggested the use of compression bandages to treat the symptoms of venous diseases, such as varicose veins and leg ulcers.³ Richard Wiseman (around 1676) was the first who treated venous leg ulcers with a (non-rubber) stocking. For this purpose he used a leather lace-up stocking. It was shaped narrower at the ankle and wider over the calf. The lace allowed the stocking to be tightened, to apply the correct amount of pressure. The treatment with elastic compression had to wait until the discovery of rubber by Charles Goodyear in 1839. As date of birth of the elastic stocking one normally takes the 26th of October 1848. On this day William Brown from Middelsex applied for a patent on a elastic stocking, woven from rubber threads which he called 'elastic stocking'. Since that time many different kinds of bandages and stockings have been applied with mixed success.

Compression therapy is nowadays widely used in the treatment of all kinds of phlebological diseases. Furthermore it is effective in the removal of oedema caused by (for example) cardiac failure and hypoalbuminemia, and in the prophylaxis of deep vein thrombosis. Compression therapy can be given by means of elastic compression bandages, elastic compression stockings or intermittent pneumatic compression (*Table 1*).

Table 1. *Type of compression*

Bandages: <ul style="list-style-type: none"> - non-elastic - short-stretch ($\leq 70\%$) - medium stretch (70-140%) - long stretch ($\geq 140\%$) Plaster bandages: <ul style="list-style-type: none"> - short stretch - medium stretch 	Intermittent compression: <ul style="list-style-type: none"> - pneumatic - manual
Elastic compression stockings: <ul style="list-style-type: none"> - made to measure - ready made 	Phased continuous compression <ul style="list-style-type: none"> - extubatio of van der Molen

In general there is no doubt about the clinical effectiveness of compression therapy in most of the indicated conditions. However, although many aspects have been investigated up to now, there is still a lot of indistinctness and a great deal of speculations about the exact working mechanism in each of the individual diseases. During the last years more details on this subject have become available. In this chapter we will review the effects of compression

therapy on venous pressure, interface pressure, tissue pressure, flow and flow-velocity, and finally the microcirculation of the skin. But first we will describe general aspects of elastic compression stockings and their effect on the clinical cutaneous symptoms in CVI.

TREATMENT OF CVI BY ELASTIC COMPRESSION STOCKINGS

Classification

At this moment there is a wide variety of stockings available for compression treatment. In the Netherlands more than 170 different elastic compression stockings are available*. All stockings have been divided into 4 different compression classes according to the Commission Européen de Normalisation (CEN).⁴ The pressure classification depends on the pressure exerted by the elastic stockings at the ankle or B region (*see figure 1*, chapter 4) of the lower leg. Most often this CEN- classification is simplified into; I) up to 25 mmHg; II) 25-35 mmHg; III) 35-45 mmHg and IV) up to 45 mmHg (*see Table 1*, chapter 3). Officially the classification is expressed in hPa, but mmHg is still being used by almost everybody in daily practice. All 4 compression classes have their specific indications, which have been summarized in Table 2.⁵

Table 2. Indications for different compression class stockings.

Indication	Compression class			
	I	II	III	IV
thrombosis prophylaxis	+			
pregnancy		+		
heaviness / tiredness		+		
light oedema		+		
moderate oedema		+	+	
strong oedema			+	
after sclerotherapy		+		
dependency		+		
varicose veins without oedema		+		
varicose veins with oedema		+	+	
mild CVI		+		
severe CVI			+	
severe CVI with oedema			+	+
healed venous ulceration			+	
post thrombotic syndrome			+	
angiodysplasias			+	
after erysipelas			+	
lymphoedema grade II			+	+
lymphoedema grade III				+
lymphoedema grade IV				+

Elastic compression stockings in the European Community are being controlled every year by the government. For pressure control 5 different pressure measuring techniques are available, out of which the French FTI technique has been chosen by the CEN as reference method.^{6,7} Furthermore the pressure profile or gradient of an elastic stockings is important.

It is generally agreed upon that there should be a pressure reduction from ankle to the hip, in the same range as the decrease of influence of gravitation.⁸ Also these European pressure profiles have been put into figure and can be seen in *Figure 1*. There is hardly any decrease between B and B1. At B1, a pressure of 80 to 100% of the ankle pressure should be given. Also the level of tolerance is defined in this figure. At the B1 level this tolerance should be 10%. This means that a compression class II stocking with an ankle pressure of 30 mmHg may have a pressure between 33 and 27 mmHg.

Knitting

A second important difference between the stockings is the way they have been knitted. Roughly two kinds of stockings can be distinguished: round-knitted and flat-knitted. The edges of the latter are sewed together and therefore have a seam on the back and are easily recognized. Flat-knitted stockings can perfectly be made-to-measure without influencing the tension of the yarns. The major advantage of these stockings is that at each centimeter along the leg the exact pressure is known. A relative disadvantage is that this stocking will only fit the patient for which it has been made, so they are expensive. Some manufacturers still knit these flat-knitted stockings by hand and some already have machinery for it. Round-knitted stockings are all being made automatically. They can only be made-to-measure by changing the tension of the yarns. So almost all these stockings are ready-made ("confection"), and not made-to-measure. The advantage of ready-made is that they are relatively inexpensive. However Mooy et al. showed that the majority patients with venous diseases do not fit these ready-made stockings.⁹ Factors that are important to determine whether one should use ready-made or made-to-measure stockings are: size of the leg, the desired slope or stiffness factor, compression class, and if flat- or round-knitted are going to be used.

Slope or stiffness factor

Elastic compression stockings are being made of natural or synthetic rubber yarns. So the stockings will have the physical aspects of the yarns used. One of the most important physical aspects of rubber is its elasticity. Natural rubber is made from the milk of the rubber tree (*Hevea Brasiliensis*). After processing, the rubber gets its elasticity as we know it from daily practice. The pressure given by an elastic yarn is related to its tension, which implies that there is a relationship between the pressure and the circumference in stockings. So, if the circumference increases, the pressure will also increase with a certain amount. Different terms are being used for this phenomenon: stiffness factor, slope or elasticity coefficient. It is defined by the CEN as: "the increase in pressure of the stocking when the circumference of the stockings increases with 1 centimeter, expressed as hPa/cm". So in other words, $\text{slope} = \Delta p / \Delta o$, in which Δp is the change in pressure and Δo is the difference in circumference. The higher the slope value of the stocking, the more the stocking will prevent the patient from having oedema. However, the higher the slope value, the more trouble the patient will have to put on the stocking. Most elastic compression stockings have a slope value of less than 4. The phenomenon slope has, up to now, not been investigated properly.

Especially the clinical relevance of the value is at this moment unclear since clinical data are lacking. Some manufacturers started to put the slope value on the selling box.

CLINICAL SYMPTOMS

Clinical symptoms such as leg oedema, leg ulceration, lipodermatosclerosis, white atrophy, but also the subjective complaints of the patient with CVI, are the most important parameters in the evaluation of compression therapy. From a practical standpoint, two consecutive phases can be differentiated: the acute (or oedema reducing) phase and a maintenance phase to continue the oedema free state.¹⁰ In the Netherlands it is common practice to use non-elastic bandages in the acute phase, because they have a better volume reducing capacity. In the English speaking countries however, one prefers elastic bandages for this.¹¹ The main purpose of the maintenance phase is to prevent recurrence of oedema. This is normally achieved by prescribing elastic compression stockings.

It has been demonstrated that compression therapy is superior to treating leg ulcer without compression under normal ambulant conditions.¹² However, although practiced by many doctors throughout the world there are hardly any 'evidence based' data available on the favourable effects of the treatment in venous insufficiency. Many studies addressing this issue were not properly controlled.¹³⁻¹⁶ The so-called Cochrane group has selected a number of publications that can be regarded as 'properly designed studies' on the effect of compression therapy on the healing tendency of venous leg ulcers.¹⁷ These studies show, that multi-layer bandages are superior to one layer, and elastic bandages applied with the multilayer technique perform significantly better than non-elastic bandages.¹⁸ Adhesive bandages are even more effective than the multi-layer bandage technique in healing venous ulcers.¹⁹ However, results are in contrast to studies from 'non-English countries' which showed better results with non-elastic or short stretch materials!²⁰ Also the famous Unna boot (non-elastic bandage) has demonstrated a bigger healing rate compared to class II elastic compression stockings.²¹ Recently, Horáková from the group of Partsch performed a study, in which they showed a significant better healing tendency of medical elastic compression stockings compared to non-elastic bandages.²² The study had however selected patient groups. Another conclusion from the study is that older patients, bigger ulcer sizes and ulcers with a long duration should better not be treated with elastic stockings at once. Finally, sequential pneumatic compression has also been demonstrated beneficial in the treatment of venous leg ulcers.²³

To our knowledge, only one study has evaluated the effect of graduated elastic stockings on non-ulcerating skin symptoms in CVI, such as lipodermatosclerosis and white atrophy. The results revealed a beneficial effect, but suffered from being combined with fibrinolytic enhancement treatment and from lack of control patients fitted with standard elastic stockings.²⁴

After healing of the venous ulceration, recurrence rates can be reduced dramatically if patients wear elastic compression stockings. After an average of 30 months wearing class III stockings, recurrence rates were 16% in the compliant group, and 100% in the non-compliant group. Another study demonstrated comparable results: 4% recurrence of ulceration in the compliant group versus 79% in the non-compliant group.²⁵ Recently it has furthermore been demonstrated that compression class III elastic stockings are significantly better in the prevention of ulcer recurrences than compression class II.²⁶ After 36-60 months the recurrence rates were 32% in class II and 21% in class III, although class II were better tolerated and worn by the patients.

Stockings also have an effect on the subjective complaints of the patients with CVI. Chant et al. found class II and III stockings so effective that a fifth of the patients on his waiting list for varicose vein surgery no longer desired an operation.²⁷ In roughly 80% of the patients, the stockings furthermore improved the subjective complaints of the patients. Even stockings with an ankle pressure of 15 mmHg seem to improve complaints like of heaviness, cramps, and pain.²⁸ However, another study failed to demonstrate the latter.²⁹ This study also included patients taking rutosides and the number of patients treated was small.

The primary aim in the treatment of patients with deep venous thrombosis (DVT) is to prevent local extension of the thrombus, or embolization to the lung. The second aim is to prevent the development of late complications such as the post-thrombotic syndrome. Only a limited number of studies have assessed the incidence of these late sequelae after a DVT. The incidence varied from 5 to 100 percent. Most of the studies are small in number and retrospective. It has been suggested that compression therapy can be effective in the prevention of acute as well as late complications after a DVT. This is by stimulating the development of collaterals, by reducing the transcapillary filtration, and by increasing fibrinolytic activity.³⁰ Partsch et al. treated a group of patients with acute DVT by early compression bandages and ambulation, beside standard anticoagulant therapy. Concerning the occurrence of pulmonary embolism, the group performed no worse than the standard treatment with bed rest and anticoagulant therapy alone.³¹

In an open long-term prospective study of 194 patients, Brandjes et al. studied the cumulative incidence of post-thrombotic syndrome after a first episode of DVT and assessed the preventive effect of direct application of a class III made-to-measure elastic stocking.³² The incidence of post-thrombotic syndrome was reduced by more than 50% in the patients wearing compression class III stockings. More than half the patients without stockings developed symptoms of the post-thrombotic syndrome, mostly within the first 24 months after the thrombotic event. Also in another prospective study from Zürich (up to 12 years after a DVT) a lower incidence of postthrombotic syndrome was found by administration of oral anticoagulants and regular compression therapy.³³

VENOUS PRESSURE

The effect of calf muscle movements on the (superficial) venous pressure is an important indication of the function of the venous calf muscle pump. The technique includes cannulation of a dorsal foot vein. The needle is connected to a pressure transducer and a recorder. First, the pressure is measured in erect position, called standing venous pressure (SVP). It is normally around 90 mmHg and corresponds to the hydrostatic pressure as has been discussed in chapter 1. Then the subject performs exercises by raising both heels of the ground. The pressure in normals will drop to about 10-15 mmHg and is called ambulatory venous pressure (AVP). After ending the exercise the pressure will rise again to around 90 mmHg. Measurement of foot vein pressure is a well established reference method to test the overall venous function of the lower limb. It is still considered as the gold standard in the assessment of venous diseases (venous insufficiency and/or obstruction). The major difference between a healthy subject and a patient with venous disease is that the latter cannot lower the AVP enough during exercise. So, the patient has a "continuous ambulatory venous hypertension".³⁴ The AVP measurement has been well correlated with the severity of the pathophysiology in CVI.³⁵⁻³⁷ It is for example a satisfactory predictor of ulceration in patients with CVI.³⁸ Other techniques which are non-invasive have been correlated with venous pressure measurement. Especially the results from foot volumetry (expelled volume in relation to footvolume) show a strong correlation.³⁹

Several studies have launched the question whether compression therapy, either by the use of bandages or elastic stockings, can influence the AVP in patients with venous diseases. Husni et al. evaluated the venous pressure at the foot in healthy subjects, patients with varicose veins, patients with acute DVT, and patients with a past history of DVT.^{40,41} He used pressure gradient stockings with a pressure at the ankle between 16 and 20 mmHg. Besides a significant reduction in venous volume in all subjects, he found a 21% improvement of the AVP only in patients with varicose veins, but not in the other 3 groups. Sommerville et al. studied the effect of wearing elastic compression stockings for a longer period of time. The SVP and AVP in healthy subjects and patients with symptoms of venous disease were used as parameters.⁴² After wearing elastic compression stockings for 2 months, a significant drop in AVP was found, but not in SVP. Measurements were taken with the stocking on. Five months after discarding the stockings, the AVP returned to the original value. Partsch performed a study about the effect of elastic and non-elastic bandages on the AVP.^{43,44} The results showed that only non-elastic bandages (so-called Fischer bandages) improved the AVP by 16%. Also digital occlusion of the greater saphenous vein did reduce the AVP. Neither compression class I or II stockings, nor elastic bandage produced any change in the AVP.

Graduation of compression from ankle to knee is another factor influencing the AVP. Graduation means that the pressure should decrease from ankle to knee (by 20-30%). Horner demonstrated a reduction in AVP while wearing gradient elastic stockings.⁴⁵ Two

types of stockings were tested, one with a low and one with a normal pressure gradient. A clear difference in reduction of the AVP between the two types of stockings was found (13.7 % and 7.4% resp.).

In an effort to avoid the influence of local pressure exerted by the stocking on the pressure measuring catheter in the dorsal foot vein, Christopoulos cut holes at the place of the measurement.⁴⁶ Direct measurements with compression class II stockings showed a statistically significant reduction in AVP (41%) in patients with superficial venous insufficiency. Wearing compression class II stockings for a longer period of time demonstrated a further reduction in AVP of 16% (measured without the stocking on).⁴⁷ One has to remember however, that cutting holes in stockings substantially changes the pressure profile and effect of the stocking.

Not all studies showed positive results of compression therapy on the AVP. Elastic stockings (30-40 mmHg at the ankle) appeared to have no influence on the SVP or AVP in patients with post-thrombotic limbs.⁴⁸ The only positive finding was a normalization of the so-called pressure swing (amplitude of the recording). Another paper reported on the influence of compression class II and class III stockings on the AVP, maximum venous pressure with exercise and amplitude of venous pressure excursion.⁴⁹ No major influence was found on any of the parameters. To get access to the measuring side, also in this study windows (up to 25cm²!) were sewn in the stockings by the researchers.

INTERFACE PRESSURE

With the term 'interface pressure', the pressure is meant between the patient's skin and for example a bed, mattress, boot, or bandage. Measurements of this kind have been widely practiced, mainly in pressure sore research, and in the evaluation of anti-pressure devices. During the last years also interest has been raised about the pressure underneath compression bandages and stockings, about how this pressure changes in time, and how much pressure should be given to attain ulcer healing. Several different techniques have been designed to study the interface pressure.⁵⁰

One of these is the Borgnis Medical Stocking (MST) tester, consisting of a long small bladder. Measurements with the MST technique have widely been performed underneath many different kinds of stockings and bandages. Much valuable information for the daily practice has become available since its introduction. Some studies launched the question how much pressure is exerted by bandages or medical elastic compression stockings. For example, when two class I stockings are being applied one over the other, the pressure of each individual stocking can be added. Elastic compression stockings provide a more constant compression (3-5% decrease after 24 hours), compared to crepe and elastocrepe bandages (29-48% pressure decrease).⁵¹ They furthermore maintain a better pressure graduation. Cornwall et al. evaluated the pressure gradients of different stockings by using the MST tester, and

correlated the results to the venous refilling time.⁵² Major differences were found between different brands of stockings. Only 3 out of 15 evaluated stockings were satisfactory. Another study using the MST tester, demonstrated that also bandages available on the UK drug tariff are in general unsatisfactory for the treatment of chronic venous diseases (at least in that time).⁵³ Callam et al. measured the pressure of three different types of compression bandages (elastic, minimal stretch and non-elastic) at certain time intervals, with the same measuring technique.⁵⁴ The elastic bandages in this study performed best. After 4 hours they still had 94% of the original pressure, compared to 70% for the minimal stretch and 63% for the non-elastic bandages. The MST tester has the disadvantage that it has a relative large sensor surface, that it is influenced by temperature, and that it is inconvenient for patients to keep it around their leg for a longer period of time.

Other devices in which a distant pressure transducer is coupled to the interface via a pressure-transmitting system have proved more successful and the flat pneumatic or electropneumatic sensors first described by Mooney have been extensively used for both clinical and research studies.⁵⁵ This instrument opened the way to the development of more accurate and sophisticated systems for interface pressure measurements.⁵⁶ An example is the Oxford Pressure Monitor MK II (Talley Group Ltd, Romsey, UK). This is a commercially available electropneumatic system for interface pressure measurements. The system consists of a pressure transducer and a digital display. It is battery operated and the instrument is fully portable. There is a good correlation with the interface pressure measured by an electropneumatic transducer, and the subcutaneous interstitial fluid pressure measured with a wick catheter.⁵⁷ With this instrument a few studies have so far been performed, mainly addressing the long term effect of elastic bandages and stockings.⁵⁸

TISSUE PRESSURE

The tissue of a limb can be divided into two compartments, the intravascular and extravascular (or interstitial) compartment. The latter consists of the soft tissue, muscles, fasciae and bone structures. The pressure in each of these parts depends on many factors. The intravascular pressure, for example, will be influenced by the arterial influx or venous outflow. Venous obstruction will increase this pressure. The difference between the intravascular and interstitial pressure is called transmural pressure. It is an important parameter because it is a crucial factor in the development of oedema. In patients with CVI, both the interstitial as well as the intravascular pressure are subject to changes.

Compression therapy has a strong influence on transmural pressure. By increasing the interstitial pressure, the transmural pressure will decrease. According to the Starling mechanism this will result in a reduced transcapillary filtration and thus in the decrease and prevention of oedema. In theory this seems all logical. It has however, up to now, only scantily been studied.

One technique for the measurement of tissue pressure is the Wick-in-needle technique. It consists of a hypodermic needle with a sidehole containing minute nylon fibers, pulled through the tip to increase the surface area of the needle tip and maintain the fluid-to-fluid interface required for measurements of tissue pressure. Subcutaneous pressure determinations in animals obtained with the wick technique range from -1 to -2 mmHg and probably measures the free fluid phase of interstitial fluid pressure.^{59,60} With this method the effect of elastic versus non-elastic bandages was evaluated. It was found that the rise in tissue pressure induced by foot movements was always greater under non-elastic than under elastic bandages. The increase in tissue pressure induced by foot movements (dorsiflexion) was 3.6 times greater under non-elastic than elastic bandages.⁶¹ It means that non-elastic (or short stretch) materials are superior in the removal of oedema.

In a properly designed study, Nehler et al. measured the effect of compression class II and III stockings on the subcutaneous pressure at the ankle in: 1) healthy subjects, 2) patients with varicose veins, 3) patients with lipodermatosclerosis with oedema, and 4) patients with lipodermatosclerosis without oedema.⁶² Baseline subcutaneous pressures were significantly elevated in patients with oedema, as compared to the other patients and healthy controls. The pressure rose significantly in the patient group with lipodermatosclerosis after applying the elastic compression stockings. No difference was found between class II and class III elastic compression stockings in this study. Recently another study focused on the effect of elastic compression arm sleeves on the interstitial fluid pressure in patients with lymphoedema of the arm.⁶³ The results showed a more than 9 times increase of interstitial fluid pressure after applying a sleeve. The pressure increase was greater in arms with high baseline pressure values than in arms with low baseline pressures. The results suggest also a better effect of compression therapy in patients with massive lymphoedema (high base line pressure).

Except for a pressure increase in the intravascular and interstitial compartments there will also be an increase in pressure in the intramuscular tissue underneath compression therapy. Intermittent pneumatic compression elevates the intramuscular pressure significantly above the pressure necessary to render muscle ischemia. However, the periods of pressure elevation are not long enough to produce any significant adverse effects, and the beneficial effects of decreased oedema fluid may be safely realized.⁶⁴

FLOW AND FLOW-VELOCITY

The effect of compression therapy on venous flow in the deep as well as superficial venous system of the lower leg has been studied in the past by many investigators. The main aim of most of these studies was to demonstrate that compression therapy reduces the incidence of DVT by temporarily increasing the velocity of blood within the veins. The increase in venous flow velocity can be seen as a result of the reduction of the venous volume.

Probably the first to demonstrate an increase in the velocity of deep venous blood flow by external compression were Stanton et al.⁶⁵ They injected an indicator substance into a collapsed venous system. Probably they measured the velocity of transport of the indicator, rather than the velocity of the blood. Spiro measured the blood flow in the femoral vein in humans with the use of a Nycotron bloodflowmeter, placing cuff flow probes around the femoral vein *in situ*.⁶⁶ External compression between 5 and 15 mmHg (above knee inflatable plastic splint) in his study caused a sustained increase (13%) in mean femoral vein flow, both in a control and the compressed limb. However, above 15 mmHg external compression the venous flow decreased in the compressed limb, but maintained at an increased level in the control limb. Also Sabri et al. reported that already application of 5 mmHg of external pressure resulted in a small increase in femoral venous flow.⁶⁷ A third method of studying flow and flow velocity in the veins is with the aid of radionuclear techniques. Studies so far performed, all show an increase in blood flow velocity in the deep venous system after applying a tubigrip⁶⁸, an antiembolism stockings⁶⁹, as well as different kinds of pressure with the aid of a five chambered pneumatic vinyl sleeve.^{70,71} However, a rapid decrease of blood flow in subcutaneous and skeletal muscle tissue after external compression using ¹³³Xe washout technique has also been demonstrated.⁷²

Lewis et al. examined the effect of compression class I stockings on the flow velocity in the lower extremities by measuring the whole leg clearance time.⁷³ A highly significant increase in clearance time in the thigh, the popliteal vein, as well as the calf was found. Another technique to measure flow velocity is the thermodilution technique.^{74,75} A constant flow of room temperature saline is infused through a catheter and blood temperature is continuously measured at the tip of the catheter. Using the mathematical formula of Fronek and Ganz, changes in blood temperature can be converted into venous flow. Measurements were performed with the leg in different positions and after inflating a sequential pneumatic stocking (50-60 mmHg).⁷⁶ Although the pneumatic stocking gave a 1.7 time increase of flow, a higher increase (4 times) was achieved by simply elevating the leg.

Venous velocity can nowadays also be measured with the aid of Duplex ultrasound. Mayberry et al. measured with Duplex ultrasound the influence of compression class II and class III on the mean peak venous flow velocity and venous diameter of the popliteal vein and common femoral vein. Both stockings produced a modest increase in peak flow velocity, and a decrease in the popliteal vein diameter (not in the common femoral vein). Performing 10 tip-toe movements induced a much greater increase of peak venous flow velocity in the popliteal vein and common femoral vein.

MICROCIRCULATION

Until the beginning of the eighties, skin changes in CVI such as lipodermatosclerosis, white atrophy, and leg ulceration, were explained by macrocirculatory changes. However, after the publications of the 'fibrin cuff hypothesis' by Browse and Burnand, explaining the skin changes by a diffusion disturbance of oxygen due to fibrin round the capillaries, the interest

in the microcirculatory disturbances in CVI began.⁷⁷ Within the last ten years several new hypotheses have been launched, all explaining the alterations of the skin by abnormalities in the microcirculation.⁷⁸⁻⁸⁰ None of these theories can however fully explain all skin changes, nor can they explain the beneficial effects of compression therapy.

Compression therapy is now recognized as an effective form of treatment for skin changes in CVI. Beside the positive effects on the macrocirculation, compression therapy also gives an improvement of the microcirculation, as has already been speculated on clinical base for a long time. During recent years many data have become available on this subject. Different techniques are nowadays available to study the microcirculation. Most important techniques are transcutaneous oxygen pressure measurement ($TcPO_2$), (video)capillary microscopy with or without fluorescence, Laser Doppler Fluxmetry and the recently introduced Laser Doppler Perfusion Imaging.^{81,82}

The microcirculation of the skin can be divided into a nutritional and a thermoregulatory part. The flow through the nutritional capillaries is small (15%) compared to the thermoregulatory vessels (85%).⁸³ Laser Doppler fluxmetry mainly measures the flux through the non-nutritional vessels, while $TcPO_2$ probably primarily reflects the function of the nutritive skin capillaries. Capillaroscopy looks at capillaries and is probably the best choice for studying the nutritional status of a certain skin area.

Transcutaneous Oxygen Measurement

$TcPO_2$ measurement is a simple, rapid, and non-invasive technique that allows the determination of local tissue oxygen delivery through the skin. The parameter mainly reflects the function of the nutritive capillaries. The $TcPO_2$ probe has to be heated to ensure maximal vasodilatation of the skin capillaries, because it has been clearly shown that $TcPO_2$ measurements are not reproducible unless the sensor is in the heated mode (44° or 45° C). $TcPO_2$ levels are significantly lowered in CVI skin changes such as lipodermatosclerosis.^{84,85} Around venous leg ulcers and white atrophy the $TcPO_2$ can even be extremely low, although measurements do not have a predictive value for ulcer healing.^{86,87}

The first study on the effect of compression therapy on the $TcPO_2$ in patients with venous insufficiency was done by Creutzig.⁸⁸ Patients with venous leg ulcers were measured in sitting position, with their legs raised and after applying an elastic compression bandage. The results showed higher $TcPO_2$ values when the leg is raised in comparison with the sitting position. Also after applying a compression bandage a marked increase of the $TcPO_2$ was found. The authors did not state which bandage they used in their study. Also another study revealed this improvement of the $TcPO_2$ after applying a non-elastic compression bandage around the leg in patients with CVI.⁸⁹ Also intermittent pneumatic compression treatment in patients with venous leg ulcers improves the $TcPO_2$ already after one hour.⁹⁰ The optimum external pressure applied to the skin to achieve a maximal increase in $TcPO_2$ seems to be 40-50 mmHg.⁹¹ This was however tested in normal subjects with a probe temperature of 37°.

The results of the long term effects of compression therapy on the $TcPO_2$ in CVI are less

promising. Control of the $TcPO_2$ after one year of treatment with compression therapy alone revealed no improvement of this parameter. In another study the effect of four weeks of intermittent compression treatment (4 hours daily) on the $TcPO_2$ was evaluated in patients with deep venous insufficiency and long standing lipodermatosclerosis. No significant improvement of the $TcPO_2$ was found.⁹² Also Nemeth did not detect any effect on the $TcPO_2$ after a course of five days of external pneumatic compression. His number of patients was however small ($n=8$). On the other hand, long term compression therapy in combination with stanazolol or vein surgery showed a significant rise of the $TcPO_2$ measurement in time.⁹³ Also, a recently published study testing different kinds of bandages in patients with venous leg ulcers showed a tendency of improvement of the $TcPO_2$ in the ulcer region in all treated groups after one month, though this was not a significant improvement. Inhalation of 100% oxygen did not influence the $TcPO_2$ parameter.

Laser Doppler Fluxmetry

Laser Doppler fluxmetry (LDF) is based on the same Doppler principle as the Doppler ultrasound devices used to study macro vascular structures. Laser light is penetrating the skin and photons, reflected by moving blood cells, undergo a frequency shift, whereas photons scattered in stationary tissues remain unshifted. The amount of laser light reflected back from the skin with altered frequency can be measured and is proportional to the volume or concentration of moving blood cells (flux).⁹⁴ This flux is expressed in arbitrary units. How deep the laser beam penetrates the skin is still a matter of debate. It seems that the laser Doppler mainly measures the flux in the thermoregulatory vessels.

Measurements of LDF in patients with lipodermatosclerosis and leg ulcers due to venous insufficiency showed a higher value compared with normal skin of control subjects.^{95,96} This increase is mainly present in patients with primary varicosity complicated by skin changes and patients with deep venous insufficiency.⁹⁷ The increase in flux has been explained by a higher volume or concentration of moving blood cells in the skin of patients with CVI.

Results of measurements underneath compression therapy are controversial. After wearing a compression class II stocking for 30 minutes, a mean decrease of 45% in skin blood flux was found. However, another study demonstrated a significant increase (28 105%) in LDF flux in lipodermatosclerotic skin after the application of a compression class II stocking.⁹⁸

Long term effects (1 year) of compression therapy in patients with CVI treated with sclero-compression therapy and compression class II-III stockings showed a diminished (though not significant) LDF.⁹⁹ This also seems to be the case after already three weeks of compression treatment. Two studies by the same author have been published on the short and long-term effects of compression therapy on skin blood flow in patients with diabetes mellitus.^{100,101} After wearing compression class II stockings for 5 and 12 months, a significant improvement of the veno-arteriolar reflex (VAR) was found. Reducing the increased capillary filtration in patients with diabetes mellitus is given as an explanation of this improvement by the author. After four years of treatment with compression therapy the results were even better.

Capillary microscopy

With the aid of capillary microscopy it is possible to study in vivo morphological changes in the skin of patients with for example venous insufficiency, diabetes mellitus and connective tissue diseases. The only method that evaluates blood flow in the nutritional capillaries with certainty is the capillaroscopy. Dramatical changes in the skin of patients with CVI have been described in the past. These changes are however quite variable from area to area on the same leg. They consist of elongated, glomerulus like capillaries with diffuse light areas surrounding the capillaries, an enlarged diameter of the capillaries in patients with mild CVI, an increased diameter of the so-called halo around the capillaries and finally avascular capillaries suggestive for microthrombi obstructing the nutritive capillaries. The oedema around the capillaries is one of the reasons for the abolished nutrition in the affected skin in CVI.

So far, as a parameter in the follow up of compression therapy, capillary microscopy has been used in only one publication.¹⁰⁰ This article deals with the subject of the long term effect of compression therapy and sclerotherapy on the skin changes of CVI. The results show that capillary thromboses found with capillary microscopy before the treatment were no longer present after one year follow-up. However, changes or improvement of the morphological alterations of the capillaries in CVI (elongation, tortuosity), did not occur.

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CHAPTER 3

AIMS OF THE THESIS

INTRODUCTION

Compression therapy by using bandages, elastic stockings, and/or intermittent pneumatic compression is the cornerstone in the treatment of venous diseases as well as in some other skin diseases. At the department of dermatology of the University Hospital of Maastricht we apply more than 4.000 short stretch, non-elastic or zinc paste bandages a year (1994*). We have about 30.000 consultations a year. This means roughly that 1 in 7 patients leaves our department with one or both legs bandaged. Most of these bandages are used in patients with leg ulceration and other skin complications, developed in the course of CVI. Furthermore many patients receive elastic compression stockings. These figures underline once again the importance of compression therapy in daily practice for the phlebologist as well as the dermatologist.

Although compression therapy is routinely used at our department and many other departments around the world, it is surprising how little data, based on scientific research, are available. Knowledge of compression therapy is mostly based on empirical data. For many years patients with venous diseases have been treated according to the prevailing fashion and ideas.¹ Today the health care changes into 'evidence based medicine', or making medical decisions on a proven basis.² The approach will lead to an efficient and cost effective medical care system. Both the medical profession and the government are convinced of the need for evidence based medicine. For phlebologists there is still a lot of work to do in this field. This thesis tries to contribute to that.

THE AIMS OF THE THESIS

- 1) What type of elastic compression stockings should be used in patients with venous insufficiency to prevent oedema (Chapter 4)?
- 2) What is the pressure at the skin and in the deep venous system, underneath different types of elastic compression stockings (Chapter 4, 5 and 8)?
- 3) How long do elastic compression stockings continue to exert an effective pressure (Chapter 6)?
- 4) Should we prefer elastic or short-stretch bandages in the treatment patients with venous insufficiency, such as a venous leg ulcer (Chapter 7)?
- 5) Can air-plethysmography be used to perform the supine venous pump function test (Chapter 9)?

PATIENTS AND METHODS

Patients

All volunteers and patients were seen at the department of dermatology of the University Hospital Maastricht. All patients were known with venous insufficiency and/or venous leg

ulceration in the past. Venous insufficiency was established by physical examination, and an additional investigation with light reflex rheography (LRR) and Doppler ultrasonography. Classification of the patients was made according to Widmer (*Table 1, chapter 1*) or by the so-called CEAP or Hawaii classification (*Table 2, chapter 1*).³⁴ Furthermore, an ankle-arm index measurement was performed on all the patients, which had to be above 1.0. As far as necessary, all studies in this thesis were approved by the Medical Ethical Committee of our hospital, and informed consent was obtained from each subject.

Elastic compression Stockings

Elastic compression stockings were used from different compression classes according to the Commission Européen de Normalisation (CEN), as shown in *Table 1*.⁵

Table 1. Official CEN classification for compression classes elastic compression stocking.

Compression Class	Indication of the pressure	Absolute pressure mmHg (ankle)	Absolute pressure hPa (ankle)	Simplification mmHg
I	Mild	15 to 21	20 to 28	< 25
II	Moderate	23 to 32	31 to 43	25 to 35
III	Strong	34 to 46	45 to 61	35 to 45
IV	Very strong	49 and higher	65 and higher	> 45

Those stockings were included in the studies that are easily available on the Dutch market, and routinely used in daily practice. Because of this, mainly compression class II and III were involved, because they represent the fast majority of stockings used in patients with venous diseases. Also the pressure profile of an elastic stocking has to be according to the CEN and is given in *Figure 1*. Measurements for the made-to-measure stockings were taken in supine position at the standardized points with the use of a measuring board (*see Figure 1, chapter 4*).

All elastic compression stockings used, were produced with one of the following knitting types:

Single face: circular-knitted stockings which are seamless and with inlaid yarns and elastic yarns.

Double face: flat-knitted stockings with a seam on the back; the stocking are made with an inlaid yarn or elastic inlaid and knitted yarns.

Double or single faced stockings which are knitted without inlaid yarns, also those with a minimum linear density of 156 dtex or more, were not used in this thesis. All elastic compression stockings used were made-to-measure. For single face circular-knitted stockings

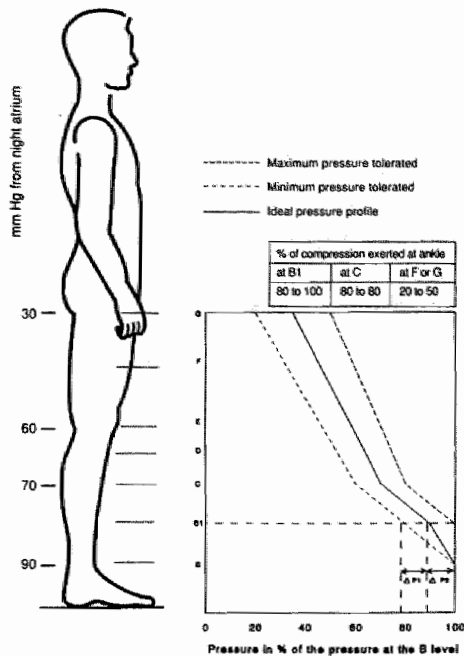


Figure 1. Pressure profile for an elastic stocking fulfilling the CEN criteria for a compression class stocking.

this was obtained by varying the tightness of courses and tension of the knitted yarns. For double face flat-knitted stockings, the form of the stockings is achieved by changing the number of needles.

Interface pressure measurements

The Oxford Pressure Monitor MKII (Talley Group Ltd, Romsey, U.K.) was used for the interface pressure measurements. It is a commercially available microprocessor controlled system.⁶ The instrument is fully portable and therefore ideal for measurements underneath bandages over longer periods of time. The technique uses sensor cells which are inflated with air, one after another. The pressure is determined inside the instrument. The Oxford Pressure Monitor MKII has a reproducibility of 4 mmHg.⁷ Twelve individual sensor cells, each with a diameter of 20 mm, can be connected to the measuring device. They are supplied in two rows of six (total length 22 cm) which can be cut apart. The total time for one measuring circle is about 20-30 seconds.

Air-plethysmography (APG)

Air-plethysmography was reintroduced by Nicolaidis and his co-workers (*see chapter 1.7*).⁸ During the past few years the popularity of air-plethysmography has increased. With the instrument volume changes of the whole lower leg can be measured. We used a commercially available airplethysmograph (APG-1000, ACI Medical, USA). It is essentially

designed for venous application and is 'users friendly'. A 36 centimeters long tubular polyurethane air-chamber is placed around the lower leg covering from knee to ankle. This air-chamber is inflated with air to 6 mmHg. It is connected to a calibration syringe, pressure transducer, and computer with a special designed software. Measurements were performed after 15 minutes of acclimatization at a room temperature between 22 and 24° C. By inflating 100 ml of air into the air-chamber a pressure-change is registered, and the system is calibrated. During the measurement all changes of limb volume cause a change in pressure in the air chamber. This pressure change is registered by the pressure transducer and 'translated' to a volume change. The results of the measurements are therefore expressed in milliliters.

The last thesis in the Netherlands that has been published on elastic compression stockings deals with a new and promising technique to determine the venous pump function in supine position.⁹ The major advantages of this technique are, that it is non-invasive, the patient can lie down for the investigation and that the room does not have to be acclimatized. The 'supine venous pump function test' is normally performed with strain gauges, with the measuring probe around the ankles. It was our intention of the final study in this thesis to investigate if we could reproduce the supine function test by using the APG. The most important reason for incorporation of the article is to bridge the two theses, both dealing with compression therapy.

TNO tester

The pressure measuring device, known as the TNO* tester, used in our study on the durability of elastic stockings is accepted by the CEN for the pressure measurement of stockings. The CEN has officially chosen for the ITF-method (ITF, Lyon, France), but several other techniques, among which the TNO-tester, are linked to the ITF method. Separate air chambers are used in the TNO tester, in which the pressure can be determined by a calibrated manometer.¹⁰ The reproducibility of the measurements has been demonstrated by TNO to be 1 mmHg. Measurements are taken at the smallest circumference of the ankle (so-called B-size; see Figure 1 chapter 4). A set of 11 different chambers is available ranging from 18 to 28 cm, referring to the B size of the patient. First the B size is marked on the stocking while the patient is wearing it. Then the stocking is taken off and pulled over the chamber. After fitting the stocking at the correct point the counterpressure is measured by pumping air into the chamber until the circumference of the stocking is the same as that of the two chamber edges. Slight handmassaging of the knitwear minimizes hysteresis forces. After a few minutes the pressure can be accurately read.

Deep venous pressure measurements

The invasive procedure was carried out in the department of Radiology in cooperation with a radiologist who is experienced in catheterization and other invasive radiological techniques. For the pressure recordings a pressure measuring catheter 18 gauge was used. Some contrast medium (Omnipaque 140) was infused to confirm the correct position of the catheter in one of the crural veins of the deep venous system. The catheter was attached to

a pressure line (Disposable Pressure Monitoring Kit, Baxter Healthcare Co, the Netherlands) and pressure measuring device (Mingograaf 62, Siemens, the Netherlands), routinely used at the department of Radiology for pressure measurements in the arterial as well as venous system.

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CHAPTER 4

EFFECTS OF MEDICAL ELASTIC COMPRESSION STOCKINGS ON INTERFACE PRESSURE AND EDEMA PREVENTION

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SUMMARY

Background: Although medical elastic compression stockings are widely used in venous diseases their effects on the venous system are still largely unclear.

Objective: To evaluate the pressure of these medical elastic compression stockings on the skin and their edema protective effects.

Methods: On 18 legs the interface pressure of the stocking on the skin was measured with the aid of an interface pressure measuring instrument (Oxford Pressure Monitor). Five different kinds of medical elastic compression stockings were used. On 12 legs the edema protective effects of the different stockings was evaluated with the use of air-plethysmography.

Results: All medical elastic compression stockings used in this study, especially the flat-knitted, showed a good pressure gradient from the B1 level upwards. High pressures were measured at the dorsal foot and the pre-tibial zone. During cuff inflation a special edema protective effect was found in the round-knitted class II stockings.

Conclusions: All class II and III medical elastic compression stockings used in this study have a sufficient pressure (especially class III) and pressure gradient for the treatment of patients with chronic venous insufficiency. Especially round-knitted stockings revealed high pressures on the danger areas such as the dorsal foot. All class II and III stockings provided an effective edema preventive effect; the round-knitted stockings have the best performance, due to their rubber components.

INTRODUCTION

Chronic venous insufficiency (CVI) is a common syndrome causing leg ulcers and other skin symptoms. The syndrome can be caused by insufficiency of the superficial, deep, or perforating system, or a combination of these. Compression therapy is a major treatment option in the syndrome. In the case of venous leg ulcerations, venous dermatitis or edema (active phase), non-elastic bandages are being used. To control the reached situation afterwards (maintenance phase) medical elastic compression stockings are normally being prescribed.¹ The effects of these bandages and stockings on the deep venous hemodynamics in patients with CVI are still largely unclear.

Several beneficial effects of compression therapy have been demonstrated. It could be shown that there is an improvement of the ambulatory venous hypertension after wearing stockings for 2 months and a decrease of the venous refilling time as measured by photoplethysmography.^{2,3} Also, positive clinical effects such as an improved ulcer healing rate and the reduction of ulcer recurrences have been documented.⁴⁻⁶ However, there are also studies that could not demonstrate a positive effect on the ambulatory venous hypertension^{7,8} nor on the venous refilling time.⁹ An objective test for the effectiveness of compression therapy is not available. In daily practice, this is evaluated by the edema preventive effect in the course of the day. It is the most widely used technique to evaluate the quality of, for example, a medical elastic compression stocking in the individual patient. It was the aim of this study to investigate more thoroughly the interface pressure and gradient provided by different medical elastic compression stockings on the skin as well as the edema protective effect.

PATIENTS AND METHODS

In the first part of the study we measured 18 legs of 10 subjects (M/F = 2:8; mean age, 62.0 \pm 17.7 years). Fourteen of these legs (eight patients) were known with recurrent venous ulceration (C₃EpPr; Hawaii classification and grading of chronic venous disease in the lower limb). Preventatively they all wore medical elastic compression stocking. All patients had proven venous insufficiency as measured with the use of light reflex rheography (LRR) and Doppler sonography. Furthermore, four legs of two venous healthy subjects visiting our out-clinic for other complaints were investigated. Both venous healthy subjects had normal LRR and Doppler sonographic measurements. All legs showed a normal arterial blood supply as evidenced by palpable pedal pulses and ankle/brachial indexes above 0.9.

All measurements were performed with five different kinds of medical elastic compression stockings (*see Table 1*). The stockings were completely new and the subjects did not wear them before the measurements. Comprinet S and Compriform are both ready-made and round-knitted. The three stockings Elvarex 2, 3, and 3 Forte are all made-to-measure and are flat-knitted, so they have a seam at the back. All flat-knitted stockings were made for each

Table 1. Different Kinds of Stockings Used in the Study.

Stocking	class stocking	Pressure at B-level
Comprinet S ¹	AES ³	± 18 mmHg
Compriform ²	II	± 29 mmHg
Elvarex 2 ²	II	± 29 mmHg
Elvarex 3 ²	III	± 38 mmHg
Elvarex 3 Forte ²	III	± 40 mmHg

¹ : Beiersdorf (Hamburg, Germany). ² : Jobst Beiersdorf (Emmerich, Germany). ³ : Antiembolism stocking.

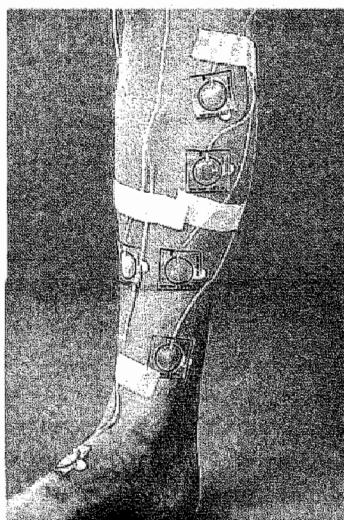
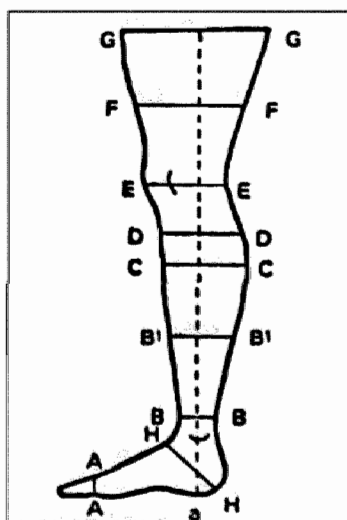


Figure 1. Diagram of the circumference sizes as indicated by the CEN. (Reprinted with permission from : Korstanje MJ, Neumann HAM. *Compressietherapie door middel van elastische kousen*. Ned Tijdschr Geneeskd 1990;134:799-802.)

Figure 2. The individual sensor cells of the OPM as they were placed at the leg.

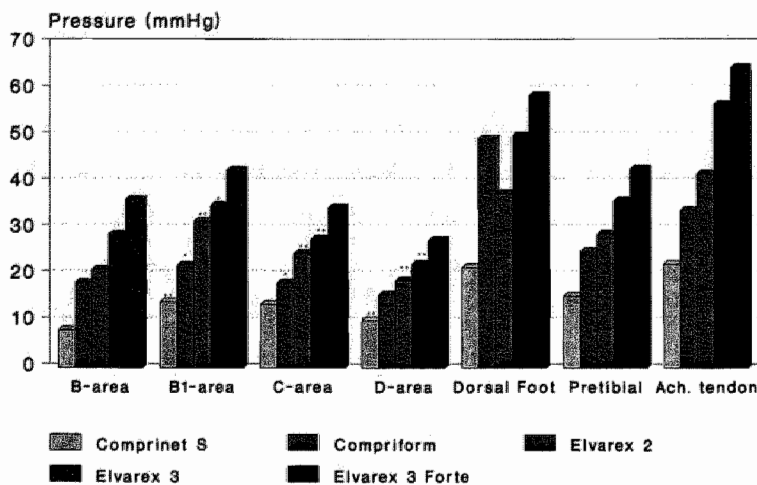
individual subject. All round-knitted stockings were chosen with the aid of the size table corresponding with the stocking.

For the pressure measurement we used a recently introduced instrument, which quite easily performs interface pressure measurements underneath compression bandages and stockings, and is called the Oxford Pressure Monitor (Talley Medical Group Ltd., Romsey, UK). It is a commercially available microprocessor controlled system for interface pressure measurements in patients. Pressure recordings have been shown to be well reproducible and accurate.¹⁰ The measuring sensors (diameter 28 mm) were placed at 12 different places at the leg: B, B1, C, and D level (medial and lateral), dorsal foot, pretibial region, Achilles tendon, and posterior at the calf (*Figures 1 and 2*).

In the second part of this study we measured 11 legs of six patients (two men and four women; mean age, 65.7 ± 10.7 years) all known with recurrent venous ulceration of the leg (C₂EpPr). The patients were examined in supine position with the examined leg slightly bent and supported by foam pads. The foot rested against a foot support, at an angle of approximately 60°. All measurements were performed with the air-plethysmograph (APG-1000, ACI Medical).¹¹ A 36-centimeter-long tubular polyurethane air chamber was placed around the lower leg, covering it from knee to ankle. This tube was inflated with air to 6 mmHg and connected to a calibration syringe, pressure transducer, and computer with specially designed software. A conical pneumatic cuff was applied at the thigh and inflated to 70 mmHg. Measurements were taken after 3 minutes of cuff inflation. In these patients we measured the total volume, first without wearing a stocking on and then after wearing each of the five different medical elastic compression stockings. Each time the cuff was carefully placed at exactly the same place. Room temperature was kept constant at 24°. Statistical analysis was performed with the use of the Wilcoxon test for paired samples and the Mann-Whitney test for nonpaired samples.

RESULTS

The interface pressure on different areas of the leg are given in *Figure 3*. The pressure at the B-level was in all stockings significantly lower than at the B1 level ($p < 0.05$, Wilcoxon test for paired samples). From B1 to D-level there was a good pressure gradient in all measured stockings. Especially in the flat-knitted stockings Elvarex 2, 3, and 3 Forte, this gradient was highly significant ($p < 0.001$, Wilcoxon test for paired samples). On the so-called danger-zones such as the dorsal foot, the pretibial zone, and the Achilles tendon a relative high pressure was expressed, especially on the dorsal foot and the Achilles tendon. On the dorsal foot this was particularly the case in the round-knitted ready-made Compriform stocking. The pretibial zone had a pressure comparable with that of the B1 level and is therefore relatively free of danger.



* $p < 0.05$; ** $p < 0.001$

Figure 3. Pressure at the skin measured at different areas of the leg underneath five kinds of elastic thera-

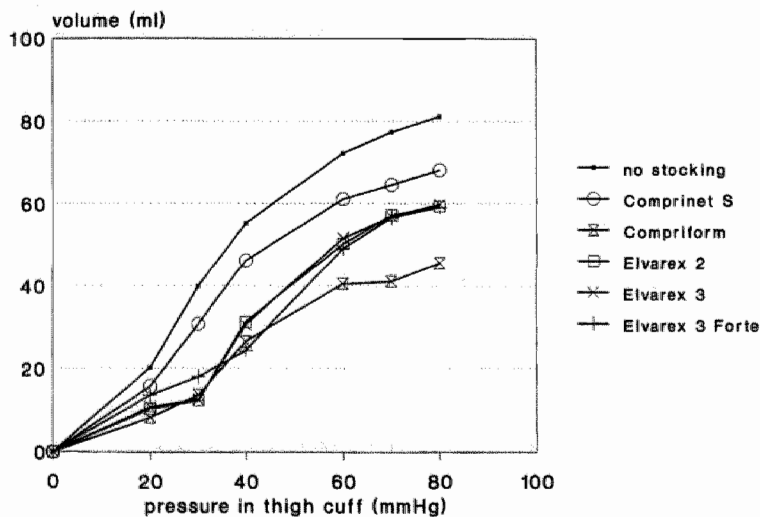


Figure 4. Volume increase with cuff inflation, without compression and with five different kinds of elastic therapeutic stockings.

Figure 4 shows the results of the calf volume increase during inflation of the thigh cuff. Particularly, the round-knitted class II elastic stocking Compriform showed a significantly smaller volume increase of the leg (edema prevention!) than without a stocking ($p < 0.05$,

Mann-Withney test). Both two stronger class stockings, Elvarex 3 and 3 Forte, showed a smaller volume increase with compression at the thigh, though not as much as the relatively lower class II Compriform stocking. The results with the Elvarex 3 and 3 Forte were, however, also significant ($p < 0.05$, Mann-Withney test). The antiembolism stocking Comprinet S showed hardly any difference in volume increase compared to no compression. So they have only very little edema protection.

DISCUSSION

The effect of a medical compression stocking depends mainly on three factors: the pressure (normally the pressure at the B-level is given by the manufacturers), the pressure gradient, and the stiffness. The latter is defined by the increase of pressure (of the stocking) if the circumference increases by 1 cm (due to edema). So, the higher the stiffness factor, the better the edema protection. The three factors mainly depend on the materials used in the stocking and the way the stockings have been sewed, ie, flat-knitted or round-knitted. Clinical significance has been well demonstrated in the past.¹² Apart from these factors of the stockings, factors of the patient also have to be taken into account when evaluating the effect of compression such as the shape of the leg, the way the stocking is handled, and of course compliance.

The results of this study have several practical implications for the daily use of elastic therapeutic compression stockings. First, the data show that the pressure exerted by elastic therapeutic compression stockings at the B-level is lower than the B1-level. This has already been reported by ourselves and others.^{13,14} It is in contrast to the manufacturers' design for pressure gradient compression stockings delivering a maximal compression at the B level. However, the manufacturers' designed stocking must ideally be measured on a completely round laboratory leg. We instead measured in vivo at the human leg, which is far from circular, especially at the ankle (*Figure 5*). According to Laplace's law ($P = T/r$, or pressure equals tension divided by the radius of the surface) the ankle anatomy has serious implications for the pressure exerted by a medical compression stocking on the skin. The flatter the surface (like just above the medial malleolus) the bigger the radius and therefore the smaller the pressure on the skin will be. We have, for example, demonstrated the clinical relevance of this in another study.¹⁵ The results showed that the pressure underneath a class II elastic compression stockings just above the medial malleolus is 27% below the average pressure of that stocking at that level. Because of all this we advise the use of pelottes (foam pads), to be placed at the medial and lateral ankle to fill the retromalleolar space. By doing this the shape of the leg will become more round, the local pressure of the elastic stocking increases, and the venous refilling time improves.¹⁶

Second, the results of this study demonstrate that all stockings used have a good pressure gradient proximal to the B1-level. Adequate compression should show a pressure fall from



Figure 5. Magnetic resonance imaging picture taken at the B-level of the ankle of a healthy subject (JV) showing that the circumference of a human leg is not round at all.

ankle to groin at least corresponding with the diminishing influence of gravitation. The European normalization for medical elastic compression stockings has made standardized ranges of pressure profiles for this (see Table 2).¹⁷ In daily practice we have the impression that flat-knitted stockings normally show a better pressure gradient than round-knitted stockings although we cannot substantiate this idea at the moment from the results of the current study. This impression is mainly based on the fact that flat-knitted stockings do not have a great elasticity in the length of the stocking and so the pressure at each centimeter along the leg is known. Furthermore, they can be made for all kind of legs, even the most disfigured legs, due to the fact that venous insufficiency and coefficient of elasticity can be changed individually.

Table 2. Standardized Ranges of Pressure Profiles for Medical Elastic Compression Stockings as Advised by the European Committee for Standardization.

Compression Class	% of compression exerted at ankle		
	at B1	at C	at F or G
Class I	80 to 100	60 to 80	30 to 60
Class II	80 to 100	60 to 80	20 to 50
Class III	80 to 100	50 to 70	20 to 40
Class IV	80 to 100	50 to 70	20 to 40

Third, the pressure measured at the skin underneath almost all medical elastic compression stockings used in this study were variable at different areas and at some point quite high. For example, they produced a continuous pressure of sometimes more than 50 mm Hg at the dorsal foot and Achilles tendon. So one has to be careful with patients having venous as well as arterial disease. These patients need specific individual attention because serious side effects of compression therapy have unfortunately been reported too often, placing the therapy in a bad light.¹⁸ One of the most important suggestions to these patients is to take their elastic stockings off at night. Furthermore, one should cope with less strong compression stockings in this group of patients or even no stockings at all (ankle-brachial index < 0.8 or an absolute ankle pressure of less than 65 mm Hg).

For the evaluation of edema prevention we used in our study the air-plethysmography (APG) because this gives an impression of volume changes in the whole lower limb, rather than only a segment as measured by strain gauge plethysmography. Another major difference is that we measured the absolute volume whereas with strain-gauge plethysmography relative (percent) changes are measured. APG has been shown to be well suitable for measurements in the horizontal position without the patient having to move his leg.¹⁹

The plethysmographic results show clear differences between the stockings used in this study. Antiembolism stockings have no value at all in the prevention of edema as can clearly be seen in *figure 4*. Class II and III indeed demonstrated an edema preventive effect although there seems to be a surprising difference in our measurements between round-knitted and flat-knitted stockings. The round-knitted stockings showed a better edema protection, which is probably due to the material used in manufacturing the stockings. Whether we can treat our difficult phlebological patients also with round knitted made to measure elastic stocking has to be evaluated in a future study.

Several other studies have also been focussed on the venous volume in correlation to elastic compression stockings. Our results are equivalent to the results of Christopoulos et al. who showed that there is a 13% reduction in venous volume when wearing an elastic stocking with a pressure of 30 mm Hg at the ankle.²⁰ Wearing these stockings for 4 weeks produced an additional 5.5% venous volume reduction in these patients.²¹ Also, the findings of Jansen et al. do underline our findings. They have studied the effect of class I elastic stockings, widely used by patients, although they do not give sufficient pressure in order to be called medical elastic compression stockings (<18 mm Hg). They also found, as we did with the antiembolism stocking, that these stockings do not have an effect on the venous capacity.²²

In conclusion, we can state that all class II and III medical compression stockings used in this study produced sufficient pressure (especially class III) and a good pressure gradient proximal to the B1 level. Because of the natural retromalleolar space, the pressure at the B-level drops underneath an elastic compression stocking and the space should be filled with a pelotte. Care should be paid to danger zones such as the dorsal foot, especially with round knitted stockings. Finally, all class II and III stockings we tested had an edema pre-

ventive effect. In future studies we have to examine this stiffness factor on the edema prevention more in detail and also the durability of the medical elastic compression stockings. Now stockings have to be controlled every 6 months and special attention has to be paid to the edema factor. We have to bear in mind however that besides all these parameters the best way to prove the beneficial effects of elastic compression stockings is to show how they prevent skin symptoms, such as leg ulcers and lipodermatosclerosis. A recent well-performed study has shown that especially class III stocking have a major place in this.²³

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CHAPTER 5

PRESSURE DIFFERENCES OF ELASTIC COMPRESSION STOCKINGS AT THE ANKLE REGION

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Dermatol Surgery (In Press).

SUMMARY

Background: Elastic compression stockings are widely used medical devices for the prevention of edema and treatment of venous diseases. Many favourable effects have been described in the past. The exact amount of pressure underneath elastic compression stockings at different areas of the leg remains controversial.

Objective: To examine the pressure at the skin underneath compression class II stockings at different places around the ankle at the B level.

Methods: Patients known with venous insufficiency and regularly using compression class II stockings (25-35 mmHg) for venous diseases were included. All subjects were wearing completely new stockings at the time of the study. Measurements were performed with an electropneumatic interface pressure measuring device (Oxford Pressure Monitor MK II) with inflatable small sensing cells. Six sensors were placed around the smallest circumference at the ankle (B-area). The highest and lowest recordings, as well as the means were evaluated.

Results: The mean pressure of compression class II stockings measured around the ankle was 24.7 mmHg (s.d. 8.4). The lowest pressures were found at the medial site: 18.3 mmHg (74% of the mean) and the highest at the pretibial zone: 33.9 mmHg (137%).

Conclusions: The pressure exerted by compression class II elastic stockings at the medial site just above the ankle (B area) is too low to have influence and improve the venous insufficiency. For the physician this is the target area. It might be an explanation for the high recurrence rate of venous ulcers even if patients are wearing stockings. Also the mean pressure of class II stockings was found to be below the normal levels of its pressure class (25-35 mmHg according to the European CEN classification). The results are advocating the use of pressure class III elastic compression stocking more often and, in addition, the use of pelottes or foam pads.

INTRODUCTION

Elastic compression stockings are widely used in the treatment of deep venous insufficiency, after vein surgery, sclerocompression therapy, and to prevent edema and deep venous thrombosis.¹ The ankle region is a most critical region, since it is the predilection place for venous leg ulcers. The compression at this place should therefore be high enough to compensate the venous insufficiency. For a good effect there should be a gradual decrease up to the knee. A lot of money is spent each year on elastic compression stockings. In the Netherlands with a population of 15 million, the total amount is over 27 million dollars each year.* Most of the stockings are being prescribed by general practitioners, followed by surgeons, physicians and dermatologists.

Elastic compression stockings are divided into four different compression classes, each with its own indication area. The stockings are categorized according to the pressure exerted at the B-area of the lower leg.² This pressure of the stockings and the quality is routinely determined in laboratory settings by the manufacturer. In Europe five different techniques for these pressure measurements are allowed.^{3,4} All 5 techniques make an assumption of a standard ideal round wooden leg of 21 centimeters (the so-called Hohenstein leg). This, however, does not resemble a human leg with its irregular shape. The irregularity will influence the pressure since pressure and radius are related according to Laplace law ($P=T/R$). It might be one of the reasons why patients still develop new leg ulcers, even if they wear their elastic stockings properly. The stockings do not perform the amount of pressure they should exert on the target area. The present study was performed to evaluate the pressure underneath widely used compression class II stockings on different areas of the ankle of the human leg.

MATERIALS AND METHODS

This study was performed in an out-clinic dermatological department where many patients with venous leg ulcers are being treated. A total of 44 consecutive patients were asked to participate in this study. All subjects were regularly wearing compression class II stockings (25-35 mmHg) for venous diseases. Many of them had a venous leg ulcer in the past (C_1).⁵ None of the subjects had edema or an active ulcer at the time of the measurements. In this study we tested the stocking, which the patient normally used. We took the measurements at the moment they started to wear a new pair of elastic compression stockings which had not been used before. For the study we included three types of stockings. The Eurostar® and Eurotex® (Varodem, St leger, Belgium) are flat knitted made-to-measure stockings whereas the Eurolux® (Varodem, St Leger, Belgium) is a round knitted made-to-measure stocking.

All measurements for the first measurement were performed in sitting position, with the leg in horizontal position. We performed a second measurement in standing position to investigate, whether this change in position might influence the pressure underneath the stocking.

*According to the FITEK, Heemstede, the Netherlands

⁵Hawaii classification and grading of chronic venous disease in the lower limb.

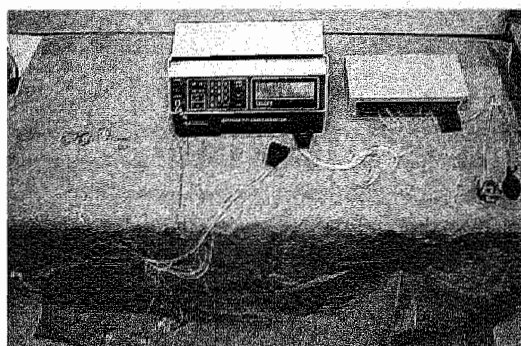


Figure 1. This picture shows the Oxford Pressure Monitor MK II (OPM), the calibration clamp and sphygmomanometer for calibration and the individual cells.



Figure 2. This figure shows how the individual cells of the Oxford Pressure Monitor were placed around the ankle.

In addition we performed measurements in 10 volunteers after 5, 10, 15, 20, 25, and 30 minutes to ensure that overstretching of the stockings (i.e. hysteresis) did not interfere with the results.

The pressure recordings were made with an Oxford Pressure Monitor MK II (OPM) (Talley Group Ltd, Romsey, UK).⁵ It is a commercially available electropneumatic system for interface pressure measurements. The system has a pressure transducer, a digital display and is battery operated (see Figure 1). The instrument is fully portable. Readings obtained have an accuracy of ± 4 mmHg. The calibration of the OPM is performed with a sphygmomanometer and a clamp delivered by the manufacturer. Twelve individual sensing cells, each with a diameter of 20 mm, can be connected to the measuring device. They are supplied in two rows of six (total length 22 cm) which can be cut apart. The pads are inflated with air one after another. The total time of one measuring circle is about 20-30 seconds. An in vivo study has shown a good correlation between the interface pressure measured by an electropneumatic transducer, and subcutaneous interstitial fluid pressure measured with a wick catheter.⁶

One row of six sensor pads was placed over the smallest ankle (B-area) region, starting from the tibial bone (see Figure 2). The pads were kept in place by plastering tape. The stocking was carefully placed over the leg and sensors, not to displace them. To improve the accuracy of the measurements it is advised to perform each time at least 15 measurements in each position. The mean of these data is automatically calculated by the OPM. Furthermore the

highest and lowest values are given instantly. The total measuring time of one patient took several minutes. All measurements were taken directly after putting on the stocking. The mean value and its standard deviation (s.d.) of all six measuring sites of compression class II elastic stockings were calculated. Furthermore the mean pressure at the anterior and medial sites of the B-area were determined. For statistical analysis we used the Student *t*-test for paired and non paired samples.

RESULTS

Table 1 shows the pressure measured at different places around the B region underneath compression class II elastic compression stockings. The mean pressure of all measurements was 24.7 mmHg (s.d. 8.4). The highest pressure was found at the pretibial area and showed a mean of 33.9 mmHg (s.d. 13.2). The lowest pressure underneath elastic compression stockings was found at the medial site of the leg and was 18.3 mmHg (s.d. 8.6). The difference between the highest and lowest pressure around the leg was found to be highly significant ($p < 0.001$; Student *t*-test for non paired samples). The mean pressures and standard deviations are visualized in Figure 3. No significant difference was measured between lying and standing position; 24.7 mmHg (s.d. 8.4) and 26.7 mmHg (s.d. 9.0) respectively (Student *t*-test, paired samples).

Also the pressure measured underneath the three different elastic compression stockings used in the study are given in table 1. No significant difference was found between them, concerning the mean pressure, as well as the pressure at the medial and pretibial area.

Table 1. Pressure underneath compression class II elastic stockings. Mean pressure of all and each individual stocking around the B-level is given, as well as the pressure measured at the pretibial area and medial side.

stocking	n	Mean pressure mmHg (s.d.)	Pretibial zone mmHg (s.d.)	Medial site mmHg (s.d.)
All stockings; lying	44	24.7 (8.4)	33.9 (13.2)	18.3 (8.6)
All stockings; standing	34	26.7 (9.0)	--	--
Eurostar [®]	21	25.6 (10.0)	36.7 (16.6)	17.9 (10.1)
Eurolux [®]	13	24.0 (6.9)	30.8 (7.8)	19.2 (7.3)
Eurotex [®]	10	23.8 (7.0)	31.8 (9.8)	17.9 (7.3)

[®] Varodem, St.Leger, Belgium.

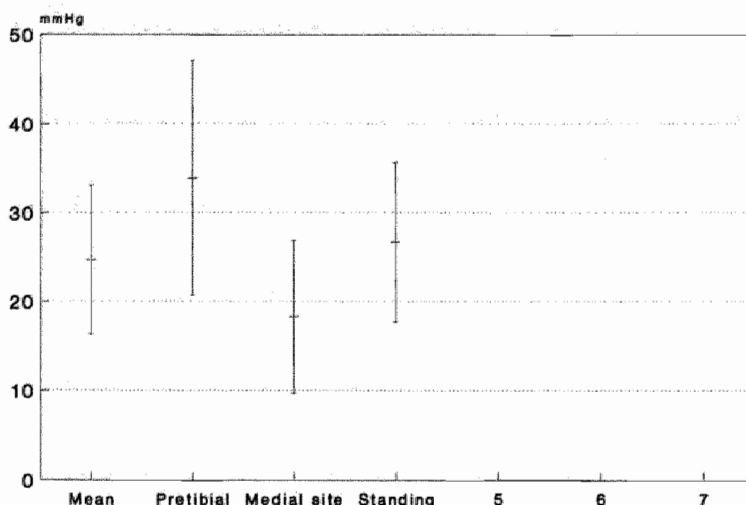


Figure 3. Figure showing the mean pressure and standard deviation of all stockings in sitting and standing position and at different places around the human leg just above the ankle (B area).

Also no significant difference in pressure was found in the group of subjects in whom we measured after 5, 10, 15, 25, and 30 minutes (Student t-test, paired samples). We can therefore conclude that our measurements taken directly after putting on the stockings were not influenced by overstrecting (i.e., hysteresis) of the stocking.

DISCUSSION

Compression therapy with the use of elastic compression stockings, or compression bandages is still considered as the cornerstone in the treatment of phlebological diseases. Elastic compression stockings were previously shown to have a favourable effect on the venous flow, venous refilling time, microcirculation and the Starling equilibrium.⁷⁻¹⁰ They do not improve the venous hypertension.¹¹ Since a complete curative surgical approach is still not possible at this moment for patients with deep, and/or perforating venous insufficiency, they all require effective compression. The main aim is to avoid complications of venous insufficiency, such as venous leg ulceration. The prevalence of severe venous insufficiency has been estimated at 8% of the total population and is therefore a great socioeconomic burden.^{12,13}

We performed this study to find an explanation for the often high recurrence rate of the venous leg ulcers even if the patients do wear their elastic compression stockings. The medial side at the B-level is in this aspect the most important area because more than 80% of all venous ulcerations of the leg occur here.¹⁴ It is the lowest point of the venous muscle pump

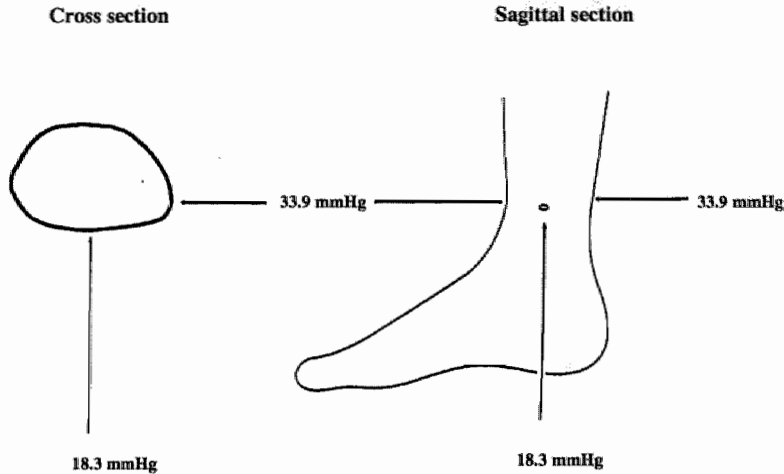


Figure 4. Cross section and sagittal section just above the malleolus (B-area) of a human leg showing the pressure at the medial / lateral site and anterior / posterior site that can be expected underneath a pressure class II elastic compression stocking.

assuming that the foot pump is working properly (which is in most patients). The results show that the pressure given by the manufacturer of the stockings was not reached in the stockings tested. The mean pressure measured around the ankle (24.7 mmHg) was just too low for its pressure class according to the CEN classification (25-35 mmHg for compression class II stockings). In standing position it increases though not significant to just above the lower border (26.7 mmHg). Twenty-five mmHg is generally accepted as the minimal pressure needed at the B-area of the leg to prevent recurrent ulceration. On the medial side only 74% of the mean pressure could be found (Figure 4). At the pretibial zone (and over the Achilles tendon) the pressure is 36% higher than the mean exerted pressure by compression class II stockings. We assumed that the stockings had a proper pressure at the start of the study. Normally stockings are being tested at random by the manufacturer and regularly also by the Dutch government.

The discrepancy between our measurements at the B-level and the pressure given by the manufacturer can be explained by differences in measuring technique. The manufacturer normally measures assuming a completely round leg with a B circumference of 21 centimeters. Another explanation is the fact that the lower human leg is at most places far from circular (*figure 4*). The more one reaches the ankle region the more elliptical the shape of the leg becomes. The tangent of the line on the skin surface becomes larger. According to Laplace's law*, the pressure exerted to the skin will therefore drop. Particularly at places where high pressures are needed, such as the medial ankle region, just above the malleolus with its perforating veins, the curve of the ellipse is flat and the pressure low. Theoretical this has been discussed a few times in the past but never been studied and proved in practice.¹⁵

* (Laplace law: $P = T/r$ or pressure equals tension divided by the radius of the surface).

We do realize that the interface pressure recording technique we used, cannot be used at sharp edges. We carefully avoided placing the sensor probes directly over the curved tibial bone and Achilles tendon. Because of this the exact pressure over the tibial bone and Achilles tendon as found in this study might in real be even higher. In practice this means that one should carefully instruct the patients to take off their stockings at night. If not, there would be a constant impairment of the local skin perfusion at the above mentioned areas with skin necrosis as a result. Also one should be carefully with prescribing stocking to persons with a complicating insufficient arterial influx.¹⁶

From the results of this study it can be concluded that many elastic compression stockings do not reach sufficient pressure at the target area (i.e., medial side of the leg). This might be one of the reasons for ulceration and their recurrences in patients who do wear their elastic therapeutic stockings in the prescribed way. We therefore advice to use stronger class III elastic compression stockings in patients who have had a venous leg ulcer. By doing this one is sure to have enough pressure at the medial side. We have for example performed the same measurements in seven patients with class III elastic stockings and found a pressure of 30.4 mmHg at the medial site (mean pressure: 37.7 mmHg and 46.6 mmHg at the pretibial site). Another possibility is to increase local pressure by using a so-called pelotte.¹⁷ This pelotte needs to have a curved surface at one side with a small radius. According to Laplace's law the pressure at the skin and hence the tissue pressure and transmural pressure will increase. It is therefore strongly suggested to treat patients with severe venous insufficiency besides surgical correction, with an elastic therapeutic stocking plus a pelotte or even better an elastic therapeutic stocking with an inbuilt pelotte. The latter are produced by some manufactures.

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CHAPTER 6

ELASTIC COMPRESSION STOCKINGS: DURABILITY OF PRESSURE IN DAILY PRACTICE

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VASA (In press).

SUMMARY

Elastic compression stockings are valuable tools in the treatment of many phlebological diseases. As to day no data are available about how long these elastic compression stockings continue to exert enough compression for a proper clinical function. In this study we measured the pressure at the B level of compression class II and III elastic stockings directly after the patients started to use them, after 1 month, and after 3 months. In total 99 below knee stockings were measured with a TNO-tester, which has officially been accepted by the CEN for measurement of elastic compression stockings.

Class II flat knitted stockings showed a mean pressure of 29.3 (s.d.4.9) mmHg at the start of the study, declining to 27.6 (s.d.5.2) mmHg, and 26.5 (s.d.4.4) mmHg, at 1 and 3 months respectively. The round knitted class II had comparable results. In class III flat knitted stockings we measured 47.5 mmHg (s.d.8.1) at the start, and 44.2 (s.d.7.1) mmHg, and 41.3 (s.d.6.7) mmHg, at 1 and 3 months respectively. Extrapolation of the results after 1 and 3 month demonstrate that the mean pressure of class II stocking is less than 25 mmHg after 4 to 5 months. Class III stockings were less than 35 mmHg close to 6 months, if evaluated in the same way. Individual regression analysis show that after 6 months 66% of the pressure class II stockings have a pressure of less than 25 mmHg and 45% of the pressure class III less than 35 mmHg. When considering a 10% safety margin the figures are respectively 84% and 63%. From the results of this study it can be concluded that, especially for the most frequently used compression class II stockings, three new stockings each year are necessary to ensure an effective function of the stocking during the time they are being used by the patient. For compression class III flat knitted stockings two pairs can be considered as sufficient.

INTRODUCTION

Elastic compression stockings are valuable tools in the treatment of phlebological diseases.⁷ Since Charles Goodyear discovered the practical use of rubber it became possible to make elastic medical equipment's. As date of birth of the elastic stocking one normally takes 26th of October 1848. On this day William Brown from Middlesex applied for a patent on a stocking, woven from rubber threads which he called 'elastic stocking'. Many different kinds of bandages and stocking have since then been applied with mixed success. Important beneficial effects of elastic compression stockings on venous insufficiency have been demonstrated in the past.^{8,9,11} Elastic compression stockings are (arbitrary) divided according to the CEN (Comité Européen de Normalisation) into four different compression classes.³ Compression class II ranges from 25-35 mmHg and is worldwide most frequently used, followed by compression class III stockings (35-45 mmHg). A pressure of 25 mmHg is generally accepted as the absolute minimum to ensure a proper (medical) function of an elastic compression stocking. However, many doctors will take a safety margin of 10% into account to be sure that the majority of their patients receive an effective treatment.

A characteristic of rubber is that it loses its elasticity in time. This is the case in a natural rubber yarn as well as the widely used synthetic rubber yarns (Spandex or Lycra®). So, also elastic stockings gradually lose their pressure necessary to prevent worsening of the venous skin symptoms such as ulceration. Therefore, elastic compression stockings have to be replaced at certain time intervals. In the Netherlands, patients receive reimbursement for new elastic stockings twice a year. The problem is however that no data are available about how long elastic stockings continue to exert enough compression to have an effective clinical function. The aim of this study was to measure the pressure of the stocking at the ankle region at different time intervals during wearing.

PATIENT AND METHODS

This study was performed in an out-patient dermatological clinic treating patients with phlebological complaints such as varicose veins, leg ulcers and skin symptoms due to venous insufficiency. Patients treated with elastic compression stockings were asked to participate in this study. A total of 59 patients (M/F: 19/40; mean age 65.3 years (s.d. 12.2 years) gave their verbal consent. All patients already routinely used elastic compression stockings for many years and were experienced in wearing and taking care of their stockings. A total of 44 patients used stockings on both legs and 15 on only one leg.

A total of 99 below knee (A-D) elastic compression stockings were included in this trial. All stockings can be classified into three different types: compression class II flat-knitted, compression class II round knitted and compression class III flat-knitted. Only the most frequently used types of stockings at our department were included in this study. All stockings

Table 1. Table giving the elastic stocking used in this study.

	Pressure class	Stocking	Number
I	Compression class II; flat knitted	Eurostar ^{®1}	35
		Eurotex ^{®1}	9
		Neotex ^{®1}	2
		Elvarex 2 ^{®2}	6
II	Compression class III; flat knitted	Euroform ^{®1}	28
		Elvarex 3 ^{®2}	9
II	Compression class II; round knitted	Eurolux ^{®1}	4
		Souplesse ^{®1}	3
		Venotrain ^{®3}	1
		Bellavar ^{®2}	2

¹ Varodem, St.Leger, Belgium. ² Jobst, Emmerich, Germany. ³ Bauerfeind, Haarlem, the Netherlands

and their compression classes are summarized in *Table 1*. Each elastic stocking was 3 times measured; 1) directly after receiving the stocking from the manufacturer, 2) after 1 month, and 3) after 3 months.

Pressure measurements were performed with a pneumatic airpressure gauge method developed by Stolk.¹² The technique is known as the TNO^{*} tester and accepted by the CEN for measuring the pressure of elastic compression stockings. The technique has been well described in the past.¹³ In short, separate air chambers are used in which the pressure can be determined by a calibrated manometer. Measurements are taken at the smallest circumference of the ankle (socalled B-size). A set of 11 different chambers are available ranging from 18 to 28 cm, referring to the B size of the patient (*see Figure 1*). First the B size is marked on the stocking while the patient is wearing it. Then the stocking is taken off and pulled over the chamber (*see Figure 2*). After fitting the stocking at the correct point the counterpressure is measured by pumping air into the chamber until the circumference of the stocking is the same as that of the two chamber edges. Slight handmassaging of the knitwear minimizes hysteresis forces. After a few minutes the pressure can be accurately read. The reproducibility of the measurements has been determined by TNO at 1 mmHg.

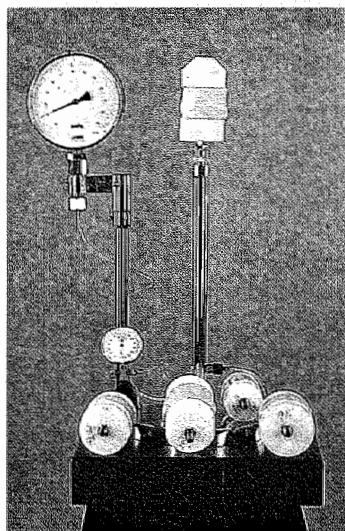


Figure 1. TNO testing device for counter pressure measurements underneath elastic compression stockings with different chambers for different B sizes of the lower leg.

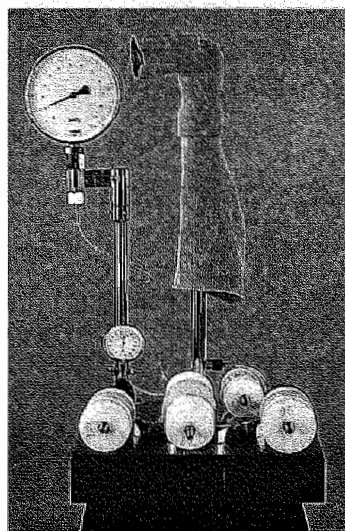


Figure 2. TNO testing device with an elastic stocking pulled over the pressure chamber.

Data are expressed as means \pm standard deviations (s.d.). Mean values regarding the pressure after 1, and 3 months were compared using the Friedman-test for 3 related paired samples.¹ In order to assess the loss of elasticity per stocking the three successive measurements (or two in case of one missing) were used to calculate individual regression lines and predict the moment of passing the lower border of their compression class (25 and 35 mmHg for respectively compression class II and III elastic compression stockings).

RESULTS

A total of 59 patients using 99 elastic compression stockings were enrolled in this study. At the time of the second measurement 8 patients (12 stockings) could no longer be evaluated; 4 patients did not want to participate any longer, 3 could not attend their visits any longer due to illness and 1 due to other reasons. At three months 3 further patients (5 stockings) could not be measured because the patients did not attend their appointments.

The means \pm s.d. of all pressure measurements is given in *Table 2*. The pressure at the B-level of class II flat knitted stockings was 29.3 mmHg (s.d. 4.9). It declined to 27.6 mmHg (s.d. 5.2) and 26.5 mmHg (4.4) at 1 and 3 months respectively. The drop in pressure was statistically significant at 3 months ($p < 0.01$; Friedman-test). The compression class II round knitted stockings showed approximately the same decline as the flat knitted stockings.

Table 2. Mean pressure and standard deviations (s.d.) underneath the different elastic compression stockings per pressure class.

Stocking	t = 0		1 month		3 months	
	N	mmHg(sd)	N	mmHg(sd)	N	mmHg(sd)
Compression class II; flat-knitted	52	29.3 (4.9)	42	27.6 (5.2)	39	26.5 (4.4)
Compression class III; flat-knitted	37	47.5 (8.1)	35	44.2 (7.1)	33	41.3 (6.7)
Compression class II; round knitted	10	28.6 (3.8)	10	27.8 (3.3)	10	26.4 (3.6)

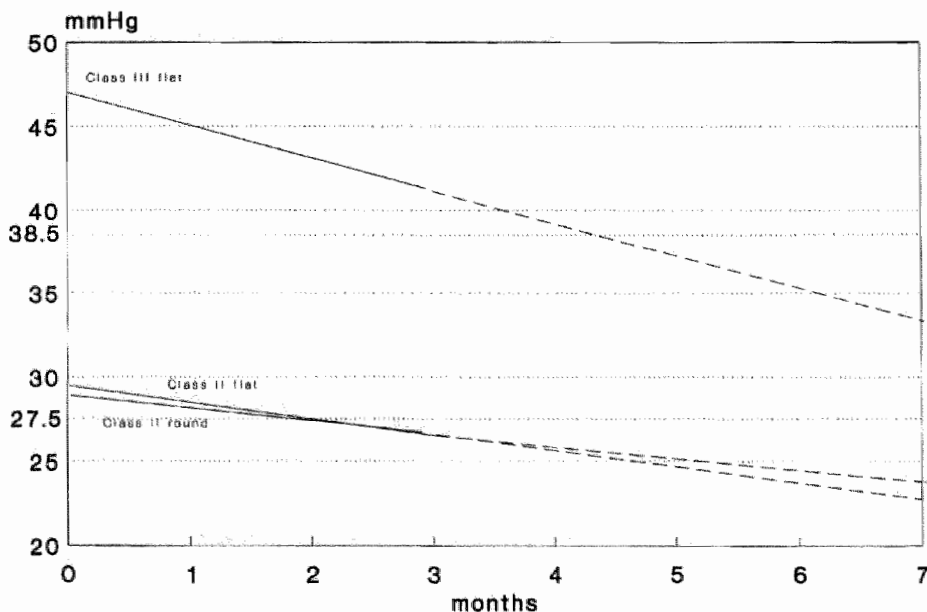


Figure 3. The mean pressure at $t=0$, after 1 and 3 months (extended line), measured underneath elastic compression stockings of different classes. Extrapolation (dotted line) indicates the time at which the stocking passed the critical lower border of the compression class.

The compression class III flat knitted stockings showed a larger decrease in the pressure: 47.5 mmHg (s.d. 8.1) at the start; declining to 44.2 mmHg (s.d. 7.1) and 41.3 mmHg (s.d. 6.7) at 1 and 3 months respectively. This drop in pressure was also statistically significant at 3 months ($p < 0.01$; Friedman-test).

Figure 3 shows the mean of the three compression classes at the three time intervals. After 3 months the mean pressure was still above the lower edge of the compression class in all three, as can be seen by the different lines. The dotted lines represent the extrapolation of the results after 1, and 3 months. It shows that the mean pressure of compression class II stockings (flat as well as round knitted) pass the critical border of 25 mmHg (according to the CEN) somewhere between 4 and 5 months. Compression class III stockings pass their critical border (35 mmHg) close to 6 months, according to the extrapolation.

Figure 4 shows the cumulative percentage of compression class II stockings with a pressure of less than 25 mmHg at each time interval. The results show that at the beginning of our study ($t=0$) 21.4% of the compression class II stockings had a pressure of less than 25 mmHg. The values left to the zero point represent the elastic stockings with a pressure far less than 25 mmHg at $t=0$. After 3 and 6 months about 32% and 66% of the elastic compression stockings had passed the critical border of 25 mmHg. The same has been put into figure when taking into account a 10% safety margin. For compression class II this means that the critical border becomes 27.5 mmHg. Then 32% of the class II stockings had a pressure of less than 27.5 mmHg at the beginning. After 3 and 6 months the figures were 65% and 84%.

Figure 5 shows the same data as Figure 4, but now for compression class III stockings. Less than 35 mmHg is normally the border at which the pressure is considered as not sufficient anymore (right line). At the time of the start of the study, about 11% had a pressure of less than 35 mmHg, and after 3 and 6 months the figures were 22% and 45%. The left line represents also a 10% safety margin (38.5 mmHg). It can be read from the figure that 15% of the class III stockings are insufficient already at the beginning. Further 43% and 63% are insufficient at 3 and 6 months.

DISCUSSION

Many patients regularly use elastic compression stockings to prevent venous symptoms, oedema, and recurrent ulceration. Replacement of these medical devices have, so far, been performed on an empirical basis. For the first time data on this subject have become available. The results of this study have several important clinical implications. It is, for example, not known how long an elastic compression stocking can maintain sufficient pressure to prevent complications of venous insufficiency like oedema and leg ulceration. In the Netherlands, and also in some other countries of the European community, patients get a

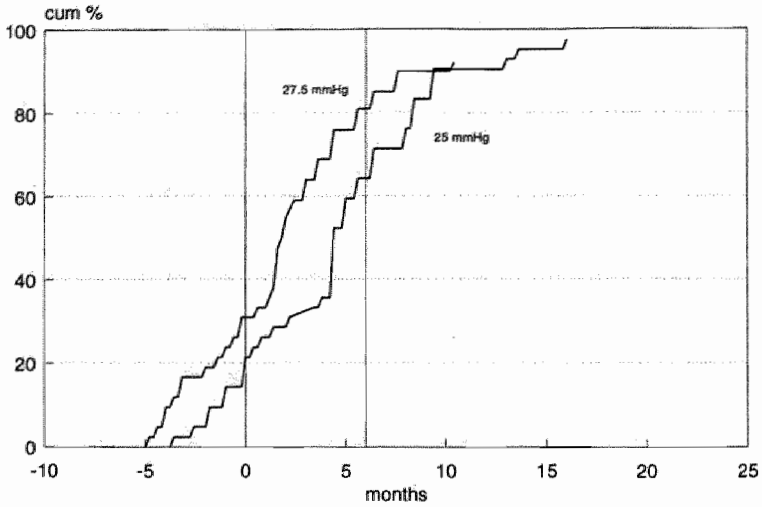


Figure 4. Cumulative percentage of the compression class II stockings measured in this study with a pressure less than 25 mmHg (right line) and less than 27.5 mmHg (taking into account a 10% safety margin). The values left to the zero point mean that these stockings have a pressure far less than 25 mmHg before the start of the study, ie, before the patient started to wear the stocking!

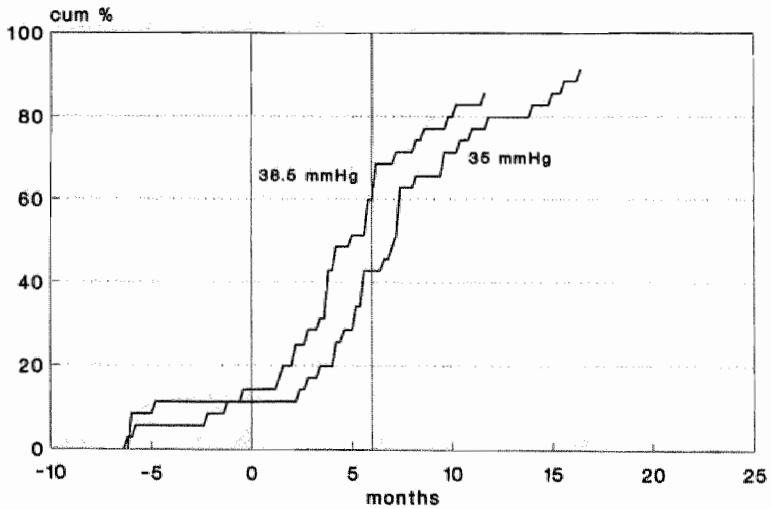


Figure 5. Cumulative percentage of the compression class III stockings measured in this study with a pressure less than 35 mmHg (compression class II) and less than 38.5 mmHg (10% safety margin).

prescription for medical elastic compression stockings twice a year, so in principle every six months. Worldwide compression class II elastic stockings are most frequently been prescribed. The results of this study demonstrate that after 6 months about 2/3 of these class II stockings have lost the pressure needed to stay in its compression class (according to the CEN standardization). So, during the last one or two months before replacement, the majority of patients will wear an insufficient medical device. On the basis of the results, we therefore advice replacement of compression class II stockings three times a year instead of twice. It is the absolute minimum to ensure efficacy of the treatment. For class III stockings the figures are somewhat better. These stockings still show a proper pressure after 6 months in 45% of cases. So in these stockings the time period of twice a year seems sufficient, if it is generally agreed that at least 50% of the treated patients should have a stocking with an effective pressure. If a higher percentage patients still need a sufficient treatment than, of course, also these elastic compression stockings should be replaced more often.

Since there is a considerable variation between individuals when evaluating elastic compression stockings, we have calculated the same data after taking a safety margin of 10% of the lower border of the pressure (27.5 and 38.5 mmHg). This will improve the doctors' confidence that the majority of his patients receive an effective treatment. As can be seen in figure 4 and 5 one should realize that in this situation the cumulative percentage curve of insufficient elastic stockings will shift to the left. This means that more stockings become insufficient in pressure within a shorter period of time, and have to be replaced sooner.

Phlebological patients need sufficient compression to improve their venous muscle pump, improve the venous refilling time, and diminish venous reflux. It could, for example, clearly been demonstrated that compression class III stockings are more effective in preventing the recurrence of venous ulcers than class II.⁵ This means that, in the current situation, patients will have a higher risk of ulcer recurrence during the last months before the replacement of their elastic stocking. So, more frequent replacement of these medical devices will probably also be cost effective. Factors influencing the loss of pressure of elastic compression stockings are: frequency of washing, kind of washing technique, use of moisturizers and creams on the skin of the leg (destructing the rubber of the stocking), outstretching the stocking while pulling it on, and damage by the fingernails. These factors can simply be overcome by good instructions from the doctor and bandagist.

Nearly 1/4 (21.4%) of the compression class II stockings were insufficient at the time the patient started to wear them. This has already been showed in the past and seems to be a constant observation.¹⁴ This lack of sufficient pressure of new elastic stockings should be taken into account, when the complaints of the patient do not improve.^{6,10} Another important factor when interpreting the results of this study is the fact that all elastic stockings tested meet the requirements of the DIN (Deutsches Institut für Normung). At this moment many 'elastic compression stockings' prescribed by doctors do not fulfil to this normalization. The results derived from this study do not apply to these kind of non-DIN elastic stockings.

There are several techniques to measure pressure underneath elastic compression stockings. At this moment the ITF technique developed in France has been chosen as the European standard.⁴ Other techniques, such as the TNO tester we used in this study, are available, and have shown comparable results.^{2,11,16} All have conversion factors, so that it is possible to compare the techniques. The main reason why the CEN has chosen for the French ITF method is because it is simple to use, needs little time to learn, and probably most important, it is inexpensive. However, also the TNO technique we used has all these advantages. It might be a good advice to phlebologists who treat patients with compression stockings to start measuring the pressure of the stockings used by their patients. This will improve the accuracy of the treatment.

In conclusion we can state that for the first time data have become available about the durability of the pressure of elastic compression stockings. The drop in pressure after 3 months is considerable in compression class II stockings (flat as well as round knitted). After 6 months 66% of these compression class II stockings and 45% of the compression class III stockings have lost too much pressure to have sufficient clinical function. For the frequently used class II stockings we therefore advise replacement three times a year, and twice for compression class III stockings. The results furthermore demonstrate that many elastic compression stockings do not have sufficient pressure at the time the patient starts to wear them.

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CHAPTER 7

SHORT STRETCH VERSUS ELASTIC BANDAGES: EFFECT OF TIME AND WALKING.

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Phlebologie 1997;26:19-24.

SUMMARY

This study was set up to evaluate the interface pressure underneath short stretch (approximately 70% elasticity) and elastic (approximately 170% elasticity) bandages at different places and at several intervals during 7 days. Furthermore measurements were taken during active walking on a treadmill at a certain speed. A total of 39 legs from 35 subjects (33 known with venous insufficiency and two healthy probands) were investigated in time. Fifteen legs of 11 healthy subjects were studied during active walking. Interface pressure recordings were made with the aid of an Oxford Pressure Measurement MK II (OPM) device. The cells were placed at twelve different areas of the leg and recordings were made in supine position. The pressure underneath the short stretch bandage showed a rapid decrease in pressure in supine position (from 80.5 mmHg to 43.6 mmHg after 3 hours, and 26.3 after 7 days). In the elastic bandages the pressures stayed high in all positions. At the Achilles tendon, dorsal foot, and pretibial area extreme high pressure were found up to 150 mmHg, continuing to stay high in the elastic bandages. During walking the maximal and minimal pressure were statistically different ($p < 0.05$) in favor of the short-stretch bandage. It can be concluded from the study that short-stretch bandages are not only safer in the treatment of patients with venous complaints, but are also more effective because of their better walking pressures.

INTRODUCTION

Compression therapy by means of bandages or elastic stockings is an effective and widely practiced form of treatment, already described and used by Hippocrates (460-377 B.C.).¹ In the early days, these bandages were all non-stretch until the discovery of rubber by Charles Goodyear in 1839.² After this date elastic bandages and elastic compression stockings became available for daily practice. Nowadays compression bandages can be divided into 1) completely non-elastic, 2) short-stretch ($\leq 70\%$ maximal tension), 3) medium-stretch (70-140%) and 4) fully elastic ($\geq 140\%$).

In many European countries non-elastic or short stretch bandages are preferred. This is mainly due to the fact that these bandages are more practical and safer to use. The pressure decreases in supine position (i.e. at night) and therefore non-elastic and short-stretch bandages can stay on at night.³ So, it is possible to treat patients once or twice a week on an outpatient basis. Besides this, they theoretically produce a higher peak working pressure than the elastic bandages.⁴ This can however not be referenced by hard data. On the other hand, in the English speaking countries elastic bandages are in favor because it is believed that they are more effective in all positions, maintain the compression for longer and mould better to awkwardly shaped legs.^{5,6}

Only little hard evidence is at this moment available about the pressure underneath different kinds of bandages. We therefore set up this study comparing two different kind of bandages, a short stretch and an elastic bandage. We measured the so-called interface pressures underneath the two different kinds of bandages. It is the pressure between the bandage and the skin. All measurements were performed in different positions and during walking on a treadmill.

PATIENT AND METHODS

We have investigated a total of 39 legs (35 subjects). All but two of these were patients, visiting our outpatient dermatology clinic for venous diseases such as varicose veins or healed venous leg ulceration. Non had active ulcers at the time of the study. In four subjects we measured both legs. Two others were healthy volunteers. On 19 legs we applied a short-stretch bandage with an elasticity of approximately 70% (Comprilan®, Beiersdorf, Germany) and on 20 legs an elastic bandage with an elasticity of approximately 170% (Elodur®, Beiersdorf, Germany).

For the study we used a recently introduced instrument, which quite easily performs interface pressure measurements underneath compression bandages and stockings, called the Oxford Pressure Monitor MK II® (Talley, Romsey, UK).⁷ It is a commercially available microprocessor controlled system for interface pressure measurements in patients. The suppliers indicate that readings obtained have an accuracy of ± 4 mmHg. Before the measure-

ment the OPM is calibrated with a sphygmomanometer and a calibration clamp delivered by the manufacturer. Different instruments have been used for interface pressure recordings in the past. In a recent study comparing different techniques for interface pressure recordings there was a large difference between them.⁸ The Talley instruments showed an acceptable reproducibility.

Bandages were applied by the same well-trained nurse. Care was taken to apply each bandage with approximately the same pressure. Recordings were made in the short stretch bandage group directly after the bandage had been applied ($t=0$), after 1 and 3 hours, and after 1, 3 and 7 days. Since the elastic bandage is normally worn for only 1 day, measurements were taken directly, after 1, and 3 hours.

Measurements during active walking were performed on an electric treadmill (LE 2000[®], Jaeger, Germany). The speed was set at 4 km/h. For this part of the study we measured 15 legs of 11 healthy volunteers (mean age 29.2 years; s.d. 9.4) who were able to walk properly on the treadmill. At random one of the two bandages was applied with the measuring sensors at medial B and C area of the lower leg. The volunteers first walked a distance of about 50 meters before the OPM was activated. The measurements were performed during about 1 minute (around 150 meters walking). After this, a second measurement was performed on the same leg, in the same way, with the other bandage. The mean, maximum and minimum pressure, as well as the standard deviations were derived from the data.

Statistical analysis was performed with the use of the Wilcoxon Rank test for paired samples and the Mann-Whitney test for non-paired samples.

RESULTS

Pressure at the skin underneath a short-stretch bandage or elastic bandage in time.

The mean pressures (and standard deviation) at all sites from the measurement underneath the two different kinds of bandages from the first study are given in Table 1. There was a (highly) significant drop in pressure (46%) at the B-area during the first 3 hours in the short-stretch bandage group ($p<0.001$, Wilcoxon Rank test). After 7 days 37% of the original pressure was left.

The same figures were found at the B1, C and D area (*Figure 1*). The interface pressure at the B level was lower than the B1 level at all time intervals. Underneath elastic bandages we found a not significant increase in pressure at the B level. The B1, C and D however revealed the same decrease in pressure as in the short-stretch group, although the differences were not as great ($p<0.05$, Wilcoxon Rank test). Also, underneath the elastic bandages the pressure at the B level was lower than the B1. Finally, there was a difference at $t=0$ between the short stretch and elastic bandages, 80.5 mmHg and 63.3 mmHg resp. ($p<0.05$, Mann-Whitney test). *Figure 2* shows the effect of both the short-stretch and elastic bandages on various so-

Table 1. Pressure underneath two different kinds of bandages, a short-stretch and an elastic bandage, at different places of the lower leg and in time.

Bandage		Short-stretch						Elastic		
Time	t=0	1 h	3 h	1 d	3 d	7 d		t=0	1 h	3 h
N	19	19	19	15	9	7		20	20	20
B area	80.5 (15.7)	53.5 (12.7)	43.6 (14.0)	36.2 (9.0)	33.9 (12.0)	26.3 (12.0)		63.3 (20.8)	67.2 (16.2)	69.6 (22.7)
B1 area	92.9 (21.2)	63.5 (23.1)	48.6 (15.0)	45.5 (9.7)	36.9 (15.0)	39.7 (3.8)		78.1 (16.6)	71.7 (16.7)	68.5 (17.7)
C area	74.7 (16.4)	52.9 (27.4)	42.0 (22.5)	35.3 (5.9)	29.9 (4.1)	31.3 (7.7)		63.9 (16.3)	56.8 (17.1)	53.1 (15.2)
D area	59.2 (16.4)	37.6 (14.4)	31.2 (9.4)	31.1 (12.3)	28.9 (7.3)	27.2 (3.6)		42.7 (18.5)	38.7 (15.4)	36.2 (13.3)
Dorsal foot	120.4 (34.9)	86.5 (27.5)	68.3 (18.9)	59.7 (21.5)	40.4 (18.8)	35.5 (17.4)		87.4 (34.0)	77.0 (28.4)	74.4 (25.9)
Pretibial area	103.5 (27.8)	69.5 (19.1)	57.7 (19.9)	56.5 (18.7)	53.1 (16.2)	40.3 (7.9)		74.2 (18.4)	66.3 (13.5)	63.8 (11.5)
Achilles tendon	147.5 (50.1)	107.5 (47.8)	89.2 (38.2)	93.3 (32.2)	82.3 (38.6)	74.8 (44.2)		122.2 (42.2)	124.4 (39.7)	129.2 (46.5)

called danger areas, prone to cause ischaemia during compression if there is a complicating arterial impairment. The pressure at the dorsal foot underneath short stretch bandages is 150% of the pressure at the B level. For the Achilles tendon this is even 183%. For elastic bandages the same figures were found. At the Achilles tendon an increase of 201% was measured.

Pressure underneath short stretch bandages and elastic bandages in during walking.

The mean pressure underneath both the short-stretch and elastic bandages were found to be equal on the B area (69.0 mmHg and 70.1 mmHg resp.) and on the C area (66.0 and 61.5 mmHg). The data are given in table 2. During walking on the treadmill the maximal pressure underneath the short stretch was significant higher than underneath the elastic bandage ($p < 0.05$, Mann Withney test). The same significant difference was found at the C level ($p < 0.05$, Mann Withney test) (Figure 3 en 4).

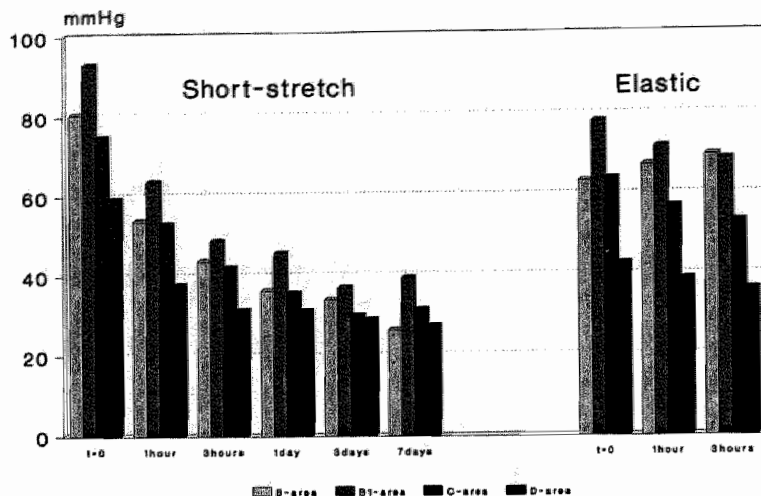


Figure 1. Interface pressure of a short-stretch bandage at different areas of the leg directly after applying, at 1, 3 hours and 1, 3 and 7 days. The same results of an elastic bandage are given at 1 and 3 hours.

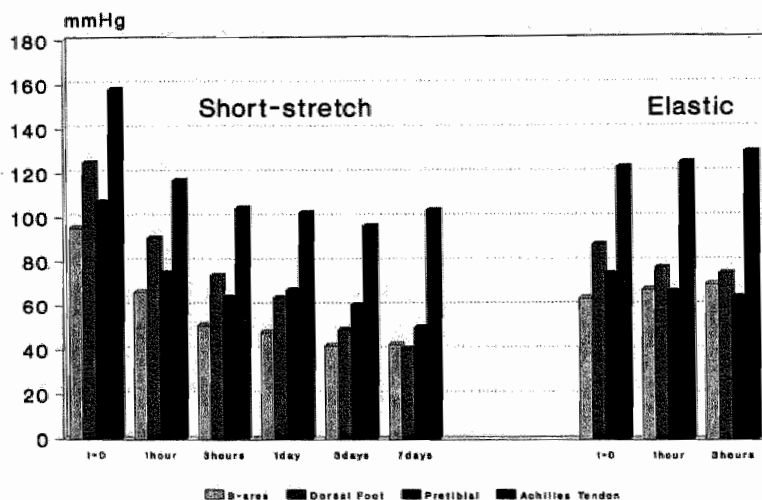


Figure 2. The same interface pressure but now at three different dangerous zones of the leg.

DISCUSSION

Compression therapy by the use of compression bandages is widely practiced in Europe, and the rest of the world. It is mainly used in the beginning of the treatment of the phlebological patient to reduce oedema and heal ulceration (active-treatment phase). As soon as the

skin symptoms have disappeared, an elastic compression stocking will be prescribed to keep the steady state (maintenance-phase). If applied by experienced people there can be no doubt about the effectiveness of compression therapy with the use of compression bandages.⁹ In several studies the beneficial effects of compression bandages on venous insufficiency and oedema reduction have been demonstrated. The venous pump function and lymphatic drainage improve, reflux in the deep veins decreases, the interstitial pressure increases, and, stated by some authors, incompetent valves close again.^{10,11} Also the microcirculation of the skin of the lower leg will improve during compression therapy.^{12,13} Furthermore there is a considerable improvement of the fluid balance. For example, while wearing an elastic stocking with a pressure of 40 mmHg at the ankle region, theoretically the transmural pressure will be reduced from 85 to 45 mmHg in standing position.¹⁴

Until now there are conflicting results comparing different kinds of bandages in the treatment of venous diseases. Only little studies have been performed so far, making a comparison of the pressure of the bandage at the skin, for example between a short-stretch and an elastic bandage. We therefore set up this investigation to perform such measurements using an established method for interface pressure measurements. The technique has originally been developed for the evaluation of mattresses, and pressure sore research.¹⁵ Small sensors used for this technique are now also available to measure smaller pressure areas, such as specific areas of the leg. Care has to be taken, not to place the sensors over areas which are strongly curved because then the data will be unreliable.

Table 2. Pressure underneath two different kinds of bandages, a short-stretch and an elastic bandage, at two different places of the lower leg during active walking on a treadmill at 4 Km/h.

	Short-stretch approximately 70% elasticity		Elastic approximately 170 % elasticity	
	Number		Number	
	15		15	
	B-area	C-area	B-area	C-area
Mean (mmHg)(s.d.)	69.0 (8.8)	66.0 (11.7)	70.1 (6.4)	61.5 (14.0)
Maximum (mmHg)(s.d.)	82.3 (12.5)	82.5 (14.8)	76.8 (6.7)*	70.6 (14.3)*
Minimum (mmHg)(s.d.)	53.1 (7.1)	44.3 (10.9)	63.2 (7.0)*	50.1 (13.0)*

* $p < 0.05$, Mann Withney test.

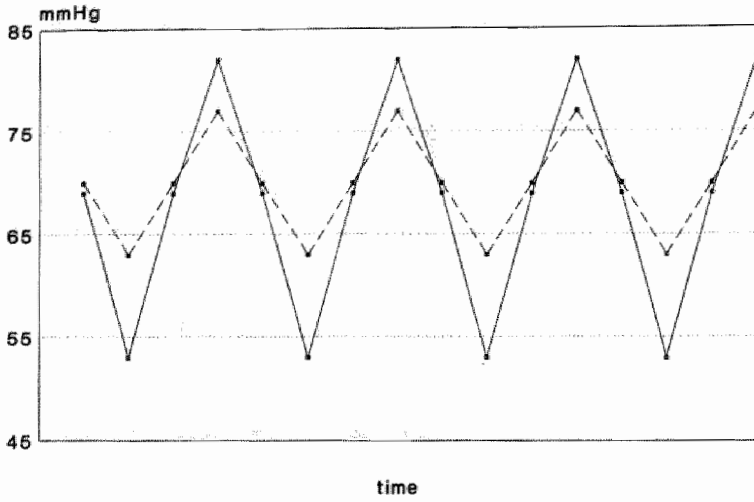


Figure 3. Maximal and minimal pressures measured underneath a short-stretch (unbroken line) and elastic bandage (dotted line) at the B-area during walking on a treadmill.

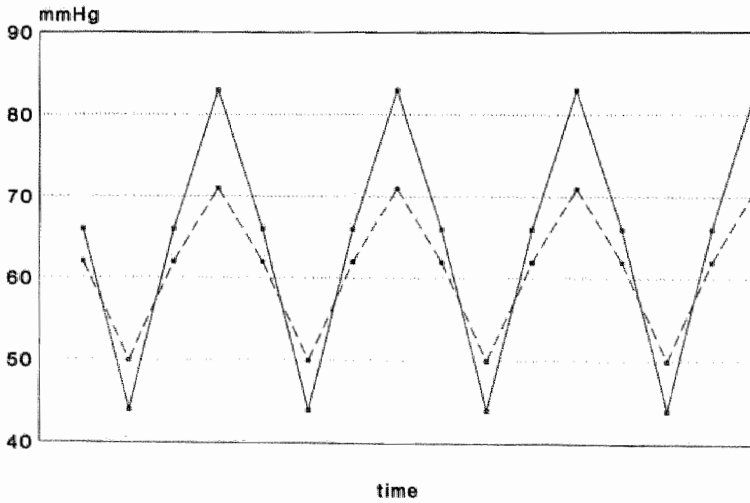


Figure 4. Maximal and minimal pressures measured underneath a short-stretch (unbroken line) and elastic bandage (dotted line) at the C-area during walking on a treadmill.

We could demonstrate a rapid fall in pressure underneath the short-stretch bandage, already 1 and 3 hours after the application of the bandage. After 24 hours, the pressure continued to drop up to 7 days, although less fast. The elastic bandages continued to exert pressure, at least at the ankle for three hours. Since elastic bandages are being taken off at night, we did not perform measurements after 24 hours. The pressure curves of both the bandages showed for most part a nice pressure gradient from the B1 area onwards. The B1 area was found to have a higher mean pressure than the B-area in both bandages. This is mainly due to the retromalleolar space where the measuring cells lie in a cavity. The higher values in the B1 area are in agreement with data from a study of Partsch who found the same results, although he measured the pressure underneath stockings.¹⁶ The results from our pressure measurements at the medial ankle are in favor of the use of pelottes or foam pads to fill the retromaleolar space and to reform the leg into a more circular object.¹⁷ High pressures were also found at areas of the lower leg that are at risk for ulceration in patients with complicating arterial insufficiency or diabetes mellitus. According to the equation of Laplace*, high pressure can be found on areas with a small radius such as the Achilles tendon, the pretibial area and the dorsal foot. It can clearly be visualized from figure 2 that in short-stretch bandages there is also a high pressure on these danger zones at the beginning of the study. However, this pressure drops after some time, even on the Achilles tendon. Underneath elastic bandages, on the contrary, the pressure is less high at the beginning, but continuous to give the same amount of pressure. Already after 3 hours the pressure on the danger zones is higher than underneath a short-stretch bandage. This might be an explanation for the frequently published data from the UK of ulceration and even amputation of the leg after the use of compression therapy.¹⁸

Our results are comparable with the results of Callam et al. who also found after 4 hours a pressure drop in the minimal stretch group and a continuation of pressure in the elastic group.¹⁹ The exact amount of "elasticity" of their bandages is however not stated in their article, so it is not completely possible to compare both studies. Furthermore they did not perform measurements after 4 hours. Callam et al. also measured a higher pressure underneath minimal stretch bandages at the beginning of the study. They felt that this is due to the fact that it is more difficult to gauge the tension in the minimal stretch bandage than in the elastic bandage, during application.

The results are also in concordance with the work of Travers et al, who performed interface pressure measurements in the same way.²⁰ They looked at self-adhesive acrylate bandages and compared this with the in their practice routinely used crevic crepe bandages. They measured at different points of time during one week, at the ankle, and calf level. After 24 hours, the same quick drop in pressure was found underneath the self-adhesive acrylate bandages, as we found in our study. After 1 day, the adhesive bandage continued to give approximately the same pressure during the rest of the week. No measurements were performed within the first day after application. The crevic crepe bandage lost almost all its pressure, already after 24 hours. Again no data of the "elasticity" of the used material was given by the authors.

* $P = T/r$; pressure equals tension divided by the radius of the surface.

An important reason why many prefer non-elastic or short-stretch bandages is the fact that they have in theory a higher working pressure than elastic bandages. In the second part of the study we were, for the first time, able to underline this theory by hard data. It can clearly be seen that the pressure measured underneath a short-stretch bandage is higher during walking. Also the amplitude of the measurement (difference between maximum and minimum pressure) is much greater in these bandages, suggesting that more blood can be pumped out of the leg. During the time that the muscles are relaxed the pressure underneath a short-stretch bandage is lower, so more blood can enter the calf veins. During the active phase the pressure is higher and more blood can be squeezed to the upper leg.

Furthermore it is stated that short stretch bandages are safer to use because they have a lower resting pressure. This can also be derived from this study. The lower pressure in rest is partly due to the inelastic material, but, much more important, it is due to the fact that short stretch bandage loose much of their pressure already after several hours. It is important to remember this while treating patients with venous leg ulcers, because 23% of these patients will have a combination of venous insufficiency and arterial impairment.²¹ In the future it might be interesting to study the difference underneath different kind of bandages during walking not only directly after the application but also after different time intervals.

In conclusion we can state from the results of this study that short stretch bandages are safer and more effective in the treatment of phlebological patients. A quick drop in pressure prevents ulcerations at areas prone to pressure ulcers such as the Achilles tendon, pretibial zone and dorsal foot. During active walking, at least directly after the bandage has been applied, the amplitude of the pressure (amplitude) will be greater than when using an elastic bandage. The lower pressure at the B level than at the B1 level found in this study, furthermore favor the use of pelottes to fill up especially the retromalleolar space and remodel awkwardly shaped legs.

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CHAPTER 8

COMPRESSION THERAPY AND PRESSURE IN THE DEEP VENOUS SYSTEM.

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J Vasc Surg (submitted for publication).

SUMMARY

Objective: To evaluate the effect of 5 different elastic compression stockings on the venous pressure in the deep venous system in supine and erect position.

Setting: Departments of Dermatology and Radiology, Academisch Ziekenhuis Maastricht, the Netherlands.

Patients: 8 legs of 7 subjects (5 patients and 2 healthy volunteers) with a mean age of 53 years (range 33-79 years) have been measured. The patients were known with extensive venous insufficiency and recurrent leg ulceration. The pressure measuring catheter was placed in one of the deep veins of the lower leg after puncturing the popliteal vein. The place of the catheter was established with contrastmedium. Then venous pressure recordings were made in supine and erect position and after wearing an antiembolism stocking, two compression class II and two compression class III stockings.

Results: All legs with stockings showed in supine position a significant increase of pressure when compared to no compression at all ($p < 0.05$; Wilcoxon Rank test). Only the stronger compression class III stockings showed a statistically significant and clinical relevant pressure increase, compared with the other 4 elastic compression stockings ($p < 0.05$; Wilcoxon Rank test). In erect position no differences in pressure were found between the legs with elastic stockings, nor when compared to no stocking.

Conclusions: The results demonstrate that only stronger compression class III stockings (> 40 mmHg at the ankle) increase the pressure in the deep venous system in supine position. Because of this, these elastic stockings can be the only stockings which have a positive influence on the pathologic deep venous system in patients with a deep venous insufficiency, such as after a deep venous thrombosis. The study confirms earlier clinical observations that in the treatment of patients with a post thrombotic syndrome and deep venous insufficiency only strong elastic compression stocking are effective.

INTRODUCTION

Chronic venous insufficiency (CVI) is a common disease. The syndrome is accompanied by severe changes of the skin such as erythema, corona phlebectatica, pigmentation and white atrophy. Patients with CVI suffer from venous reflux in the superficial, deep, and/or perforating venous system resulting in a high ambulatory venous pressure. The main reason for this are incompetent vein valves. Epidemiologic studies have estimated the prevalence of severe venous insufficiency between 6-8% and leg ulcers between 0,5% and 1% of the total population.^{1,2} About 85% of these leg ulcers are venous leg ulcers.³

Compression therapy is the cornerstone in phlebology, either as monotherapy, or as part and support of sclerotherapy, or surgical treatment. If applied by experienced people there is no doubt about its effectiveness.⁴ Compression therapy has already been used for many centuries in the treatment of oedema and ulceration of the lower leg. Already from the ancient Egypt times and from the bible there are papers which deal with the subject.⁵ During recent years many aspects concerning the positive effects of compression therapy have been elucidated. There is, for example, an established increase of blood flow velocity, expelled volume, and transcutaneous oxygen tension, decrease of transmural pressure, and improvement of ulcer healing.⁶

The absence to lower the ambulatory venous pressure in the veins of the lower leg during exercise is the ultimate cause of almost all venous pathology.^{7,8} It is called continuous ambulatory venous hypertension. The pathologic condition can ideally be measured with dorsal foot vein pressure measurements (phlebodynamometry) which still is considered as the gold standard.⁹ Also the pressure in the deep veins, such as the posterior tibial, and popliteal vein, have been measured in healthy as well as patients with venous insufficiency.¹⁰⁻¹² These observations confirm the above mentioned statement.

There is still a lot of controversy about how compression therapy can improve the ambulatory venous hypertension and what is the influence of compression bandages and stockings on the venous pressure.¹³ Since venous pressure is the major functional alteration in patients with venous diseases we set up this study. So, in this study we measured the pressure in the deep venous system in supine and erect position, without compression and while wearing 5 different elastic compression stockings.

PATIENTS AND METHODS

A total of 5 patients and 2 venous healthy volunteers (all male) were involved in this study (mean age 53 years; range 33 to 79 years). All subjects gave their written informed consent in this study which had been fully approved by the Medical Ethical Committee of our hospital in January 1996. All 5 patients were known at our department of dermatology for recurrent leg ulceration due to CVI. At the time of the study none had active ulceration and all patients were routinely using elastic compression stockings. Routine venous examination

Table 1. Bandages and stockings used for the study and the interface pressure at the B and C area.

Elastic compression stocking		Compression Class	Knitting	B-area*	C-area**
Comprinet S ^{§1}	[AES]	AES	round	± 18 mmHg	± 14 mmHg
Compriform ^{§2}	[Cof]	II	round	± 29 mmHg	± 18 mmHg
Elvarex 2 ^{§2}	[El2]	II	flat	± 29 mmHg	± 25 mmHg
Elvarex 3 ^{§2}	[El3]	III	flat	± 38 mmHg	± 28 mmHg
Elvarex 3 Forte ^{§2}	[El3F]	III	flat	± 40 mmHg	± 35 mmHg

* As indicated by the manufacture and measured with the Hohenstein tester. ** As measured in a previous study.²³

^{§1}: Beiersdorf, Hamburg, Germany. ^{§2}: Jobst Beiersdorf, Emmerich, Germany.

had revealed insufficiency of the popliteal vein in the patients besides insufficiency of other veins (deep and superficial). All had a venous refilling time of less than 20 seconds as measured with light reflex rheography (LRR). Both the healthy volunteers had no venous complaints, nor had they signs of varicosity or venous insufficiency, as checked by venous Doppler ultrasonography and LRR.

The invasive procedure was carried out in the department of Radiology in cooperation with a radiologist (TKO) who is experienced in catheterization and other invasive radiological techniques. The skin of the popliteal fossa was sterilized and the area above the popliteal vein infiltrated with 1% lidocaine for local anesthesia. After this a sterile sheet was used to cover the place. With a blade #11 knife a small nick was made in the skin overlying the popliteal vein. Through this a thin walled one piece needle 18 gauge was introduced. Once the vein had been punctured, a J guide wire was advanced into the hub of the needle. After the guide wire had been advanced safely in the vessel the needle cannula could be removed. Over the guide wire the pressure measuring catheter 18 gauge was introduced. The guide wire was removed. Then some contrast medium (Omnipaque 140) was infused to confirm the correct position of the catheter in one of the crural veins of the deep venous system (see figure 1). After this the venous catheter was flushed and attached to a pressure line (Disposable Pressure Monitoring Kit, Baxter Healthcare Co, the Netherlands) and pressure measuring device (Mingograaf 62, Siemens, the Netherlands). Finally the catheter was fixed to the skin with an adhesive bandage (Opsite).

The position of the tip in relation to the right atrium was calculated and the pressure measuring unit was calibrated with the patient in supine position. After this calibration proce-



Figure 1. Phlebogram showing the tip of the catheter in position in the deep veins.

ture, the pressure was measured in quiet lying position and in standing position. Between each measurement a time interval was taken to let the pressure stabilize for some time. Then, consecutively, five different kinds of elastic compression stockings were pulled over the leg. The specifications of each specific stocking given in *Table 1*. All stockings were made-to-measure for each individual subject. The pressure in quiet supine position was determined, as well as the pressure in quiet standing position.

After measuring the intravenous pressure of each stocking the subject was placed back in supine position. After pulling off the stocking the pressure was checked again after some time and had to be the same as at the start of the measurement. Also, after ending all measurements again the final pressure was compared to the pressure at the start. Finally the catheter was

taken out of the vein and a cottonwool compression was placed over the wound followed by a non-elastic bandage. The subject was instructed to keep the bandages on for two days.

Data are expressed as mean \pm s.d. Mean values regarding the pressure were compared using the Wilcoxon rank test for non-paired samples.¹⁴

RESULTS

In total we were able to measure the pressure successfully on 8 legs of the 7 subjects. Two times we failed to puncture the popliteal vein and in one occasion the short saphenous vein was punctured and the procedure was stopped. Non of the subjects had a bleeding from the puncture site or deep venous thrombosis after the study had been carried out, nor had any of the volunteers complaints.

The mean data \pm the standard deviation (s.d.) of all pressure recordings in the supine position are given in *Table 2*. All measurements underneath the 5 different stockings revealed a statistically significant increase of the pressure in the deep veins. The mean pressure in the deep veins increases with 20% ($p < 0.05$) after the subject has pulled on an anti-embolism stocking. For compression class II (Cof and Elv2) the mean increase in pressure is 31% ($p < 0.05$), and for the strong compression class III (El3F) even 75% ($p < 0.01$).

Table 2. Mean pressure, standard deviation (s.d.), and range of the data in the deep venous system in quiet supine position while wearing different kind of elastic compression stockings.

Elastic compression Stocking	Mean pressure (mmHg)	s.d.	Range (mmHg)
No compression	15.25	2.92	11-20
AES	18.37	4.50	11-26
Cof	20.13	4.39	14-28
EI2	20.00	4.34	14-27
EI3	21.50	3.74	16-27
EI3F	26.75	5.92	17-34

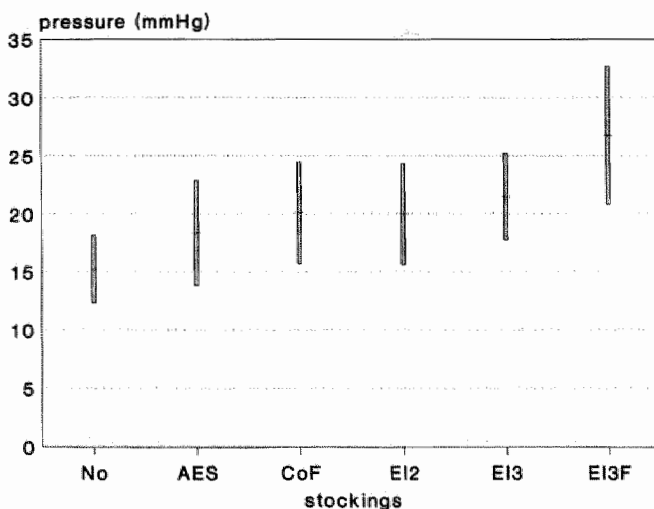


Figure 2. Mean pressure and s.d. in the deep veins while wearing 5 different elastic compression stockings.

It can clearly be derived from *Figure 2* that the highest increase in pressure was measured while the subject was wearing the EI3F. This stocking also differed significantly in mean pressure-increase compared to the other 4 stockings ($P<0.05$). These other 4, (AES, Cof, EI2 and EI3) did not show a significant difference between each other in pressure increase. *Figure 3* shows the absolute increase in mmHg of the pressure in the deep veins when wearing the elastic compression stockings.

Table 3 shows the same results but now in standing position. There is a significant difference between the supine and standing position. However, the pressure measured in the deep venous system while wearing elastic compression stockings showed no significant difference between any of the groups.

In this study we failed to perform proper measurements while the patients were performing tip-toe movements, to study the effect of different types of elastic compression stockings on the ambulatory venous pressure.

Table 3. Mean pressure, standard deviation (s.d.) and range of the data in the deep venous system in standing position while wearing different kind of elastic compression stockings.

Elastic compression	Mean pressure	s.d.	Range
Stocking	(mmHg)		(mmHg)
No compression	71.6	12.5	54-88
AES	70.7	13.5	52-87
Cof	72.8	15.6	51-98
EI2	71.4	13.3	50-84
EI3	73.5	15.8	52-94
EI3F	74.4	14.6	54-94

DISCUSSION

Dorsal foot vein pressure measurement is still considered as the gold standard in the investigation of venous diseases. It gives excellent information on the function of the venous muscle pump. Various studies have addressed the question whether compression therapy can affect the venous pressure in CVI, but the results are conflicting.^{15,16} Some investigators found an improvement of the ambulatory venous pressure (AVP) up to 41%.¹⁷ Others however found no improvement at all.¹⁸ When interpreting the results of these studies, it is the question whether pressure measurements in the superficial venous system are representative for the pressure in the deep veins, especially when evaluating compression therapy. As has been shown by radiography, the epifascial and subfascial veins become narrowed underneath compression. This will, of course, interfere with the measurements.¹⁹ Furthermore, in some studies windows (up to 25cm² !) were sewn in the stockings, to get access to the measuring side, ie, the dorsum of the foot. Such manipulations have a tremendous negative effect on the function of the elastic compression stocking.²⁰ So this means that only reliable pressure measurements can be performed underneath compression stockings, if the entrance of the cannula to the deep veins is above the stocking, such as we performed in this study. These direct measurements of the venous pressure in the deep venous system, underneath different types of elastic compression stockings, have so far never been performed.

Direct venous pressure measurements in the deep veins without compression have nevertheless been carried out in the past.¹⁰⁻¹² Our results of the pressure measurements without compression are in total agreement with the results of these previous studies. In a recent

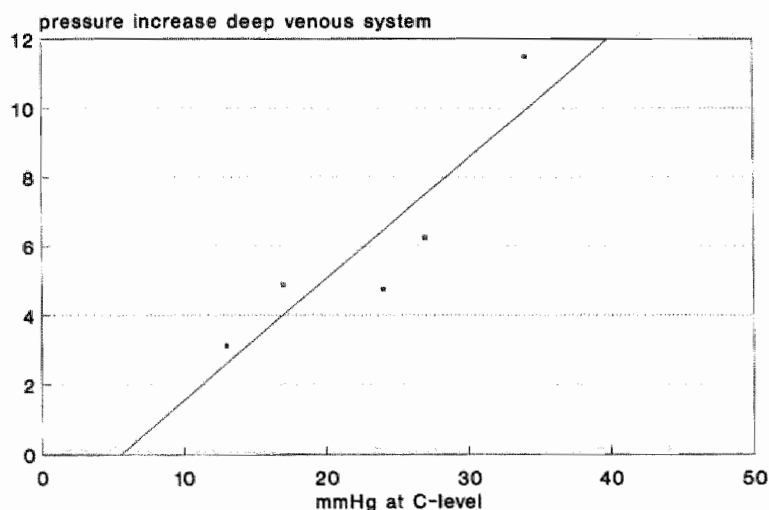


Figure 3. Correlation between the mean increase in pressure in the deep venous system and the pressure measured underneath the elastic compression stocking at the C-level (level of the tip of the catheter in the deep system in our experiments).

study Alimi et al. measured the pressure in the popliteal vein.²¹ They found a mean pressure of 14.6 mmHg (s.d. 3.9) in supine position and 39.2 mmHg (s.d. 5.6) in standing position. The pressure in the supine position completely matches ours. The standing pressure is somewhat lower than we found which is caused by the fact that they put the tip of the catheter at a higher position (popliteal vein!), so the pressure will be less in standing position.

From the results of the current study it is clear that patients with insufficiency of the deep veins, such as after a deep venous thrombosis, need strong compression to compensate their venous insufficiency, so elastic compression stockings with an ankle pressure of at least 40 mmHg. With the use of these compression class III stockings, insufficient working valves will become functional again, as mentioned by some. Main factors in this are compression and decrease in diameter of the vein. A decrease in vein diameter and decrease in venous volume by compression therapy will furthermore lead to an improved venous ejection volume. The latter will lead to an improved venous drainage and refilling time thus compensating for the venous insufficiency. However, this all can only be the case if the pressure exerted by the stocking is high enough. One should pay attention to the fact that the exerted pressure of the stocking will be absorbed by the tissues of the lower limb (skin, fat, muscle, bone). Therefore, there will be a certain pressure loss along the radius of the limb. Elastic stockings from compression class I and II have therefore no or little effect on the pressure in the deep veins.

In our study we could demonstrate a positive effect of compression stockings on the pressure in the deep veins only in supine position. In standing position the pressure was equal in all measurements, compression or no compression. This could be expected because of the so-called hydrostatic paradox, a well known phenomenon in medical physics. In our setting it means that during quiet standing the valves in the veins are always open and the pressure is equal, regardless the diameter of the vein. A major aim for a future study is to measure *dynamic* ambulatory venous pressure measurements in the deep veins with different compression stockings on. In the present study we failed to do this because of technical reasons.

In the last column of *table 1* the pressure at the C-area of each individual stocking is given, measured in one of our previous studies.²² It is clear that there is a significant and important pressure difference (measured at the skin) between EI3F and the other four tested elastic stockings. This might be a good explanation for the differences found in mean pressure increase in the deep veins in the current study. *Figure 3* shows a positive correlation between the pressure, measured at the C-level, and in the deep veins. Also this indicates that an effective compression treatment in CVI can only be reached with elastic compression stockings with a ankle pressure of at least 40 mmHg. One of the disadvantages of these stronger stockings is the fact that patients have difficulties pulling them on and off. Many patients with venous diseases are older or have rheumatoid arthritis. An advice can be to use two stockings from a lower compression class, one over the other.²³

Direct pressure measurements in the deep veins underneath antiembolism stockings have so far never been performed. A small increase in mean pressure while wearing these stockings

was found in the supine position (*Figure 2*). In the erect position no increase was measured. The latter means that antiembolism stockings play no role in the treatment of venous insufficiency. Although they are still used by many physicians, this has already been demonstrated in previous studies.^{24,25}

In conclusion, we can state that there is a difference between compression class I, II and III elastic stockings on how they influence the pressure in the deep venous system. All stockings showed a statistically significant increase in mean pressure, when compared to no compression. However, only stronger compression class III stockings with an ankle pressure of at least 40 mmHg, showed a clinically relevant increase. These results could only be found in the supine position. In erect position no differences were measured, which is in accordance with the hydrostatic paradox. On the basis of the current results we advise compression class III elastic compression stockings (> 40 mmHg) in the treatment of patients with venous reflux in the deep venous system of the lower leg and thus in all patients with a post thrombotic syndrome. Further advantages of compression class III stockings is that they have a proven increased venous pump function (measured by water-plethysmography) and less recurrences of venous leg ulcers in patients wearing also compression class III stockings.^{25,26} Furthermore they have shown a better durability of pressure in time, and produce more pressure at the medial site of the ankle, the most important area for venous ulceration, and thus the target area for prevention.^{27,28} Stockings with a pressure of less than 25 mmHg (including antiembolism stockings) should furthermore only be used for thrombosis prophylaxis in the lying position.

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CHAPTER 9

SUPINE VENOUS PUMP FUNCTION TEST PERFORMED WITH AIR-PLETHYSMOGRAPHY

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SUMMARY

Assessment of the venous muscle pump function is essential in phlebology. Several non-invasive techniques have been described in the past, such as the supine muscle pump function test. The object of this study was to perform this test with the use of air-plethysmography. In this way we measured 18 healthy volunteers, 21 patients with varicose veins and 6 patients with recurrent venous leg ulceration. There was no major difference in the results as measured in the three groups. Furthermore the spreading of the data in all three groups was high. So, although air-plethysmography has the advantage that it measures volume changes of the whole lower limb we concluded that it cannot discriminate between health and pathology in the supine venous pump function test.

INTRODUCTION

The measurement of the effect of calf muscle exercise on superficial vein pressure is an important test of calf pump function and an indication of the severity of the physiological abnormality.¹ Calf muscle pump function has for example been correlated to venous ulceration.² The gold standard in the investigation of the venous calf muscle pump function is the (invasive) ambulatory venous pressure measurement in the dorsal foot in the upright position.³ Because nowadays non-invasive techniques are in favor, new techniques have been introduced during the last few years, which correlate well with this gold standard, such as foot volumetry, light reflex rheography (LRR) and digital-photoplethysmography (D-PPG).^{4,5,6} Another new technique is the so-called venous muscle pump function test in the supine position. It has been described by van Gerwen and colleagues.⁷ The main advantages are the comfortable position of the patient, less time consuming, no thermal influences and most important elimination of the gravity. With this technique mainly the function of the deep venous system is measured. The investigators used strain-gauge plethysmography (SGP) on the foot for the measurement of volume changes, from which they calculate the pressure changes using individual volume-pressure curves.

Air-plethysmography (APG) has also recently been reintroduced by Nicolaides et al. for the measurement of venous disease.⁸ The authors conclude that the major advantage of this technique is the possibility to measure complete calf volume changes as a result of exercise in absolute milliliters, overcoming the limitations of segmental devices such as strain-gauge plethysmography and waterplethysmography.⁹ Because of these advantages, it was our aim in this present study to evaluate whether the APG could be used in the supine muscle pump function test.

PATIENTS AND METHODS

Thirty-eight legs from 30 subjects were recruited for this study. The mean age of the subjects was 57.9 years (s.d. 19.7 years). All patients were known at our department of Dermatology for either varicosity or recurrent venous leg ulcers. Venous insufficiency was demonstrated by the use of light reflex rheography (LRR) and Doppler investigation. Arterial disease was excluded by performing an ankle/arm ratio which was in all patients more than 0.9. The healthy subjects were patients, visiting our outpatient clinic for other complains than venous diseases, or students. Venous investigations in these patients were all normal.

We performed the same measurement setup as described by van Gerwen et al.¹⁰ Shortly, all subjects were investigated in supine position with the examined leg slightly bent and supported by foam pads. The foot rested on a foot support, at an angle of approximately 60°. All measurements were performed with the air-plethysmograph (APG-1000, ACI Medical, USA). A 36 centimeters long tubular polyurethane air-chamber was placed around the lower

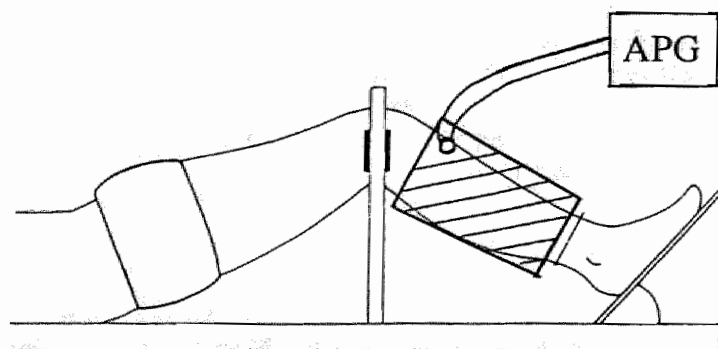


Figure 1. Schematic drawing of the position of the leg, upper thigh cuff, cuff of the APG and foot support.

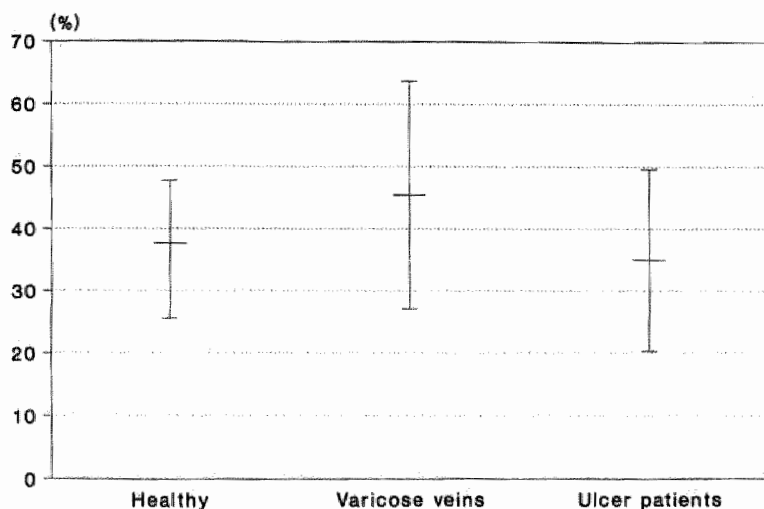


Figure 2. Diagram of the results showing the mean and standard deviation in healthy ($n = 11$), varicose patients ($n = 21$), and venous leg ulcer patients ($n = 6$).

leg covering from knee to ankle (*Figure 1*). This tube was inflated with air to 6 mmHg and connected to a calibration syringe and pressure transducer and to a computer with a special designed software.

A conical pneumatic cuff was applied to the thigh and inflated to 70 mmHg (Pc). After reaching maximal volume the patient performed 10 forceful standardized dorsoflexions with

his foot. The decrease in volume is called expelled volume. Then a pressure-volume curve of each individual subject was made. With this pressure-volume curve it is possible to convert the expelled volume into a pressure decrease. A muscle pump function can be determined by calculating the next formula: $Pf = (Pe / Pc) \times 100 \%$.

Statistical analysis was performed with the use of the Mann-Whitney test for non-paired samples. We placed the level of significance at 95%.

RESULTS

The venous refilling time as measured by LRR was shortened in almost all varicose patients and patients who had a venous ulceration in the past; 12.8 seconds (6-28) resp. 11 seconds (5-20). Doppler ultrasonography showed reflux in superficial veins in all of the varicose patients and reflux in the superficial combined with the perforating and/or deep veins in the ulcer patients. Since standard APG investigation (venous filling index, expelled volume and venous outflow) was not the primary aim of this study and APG is not routinely performed at our department, only some of the patients were measured in this manner.

The results of the expelled volume and venous pump function measurements in healthy subjects and venous patients are given in *Table 1*. The group venous healthy subjects had a mean Pf of 37.64 (s.d. 12.07), the varicose group a Pf of 45.43 (s.d. 18.29) and ulcer patients 35.00 (s.d. 14.62). There was no significant difference between healthy subjects and patients with varicose veins ($p=0.203$) nor between healthy subjects and patients with venous ulcers ($p=0.65$). From *Figure 2* it is clear that there is a great overlap in all three measured groups.

Table 1. Results of the supine venous pump function test measured with air plethysmography in the three groups tested.

Subject	N	Mean	Std Dev	Max	Min
healthy	11	37.64	12.07	59	18
Varicose veins	21	45.43	18.29	77	11
venous ulcer	6	35.00	14.62	59	14

DISCUSSION

Leg ulceration and severe varicose veins continue to be an important epidemiological problem, with a prevalence up to 1% and 8% respectively.¹¹ All these patients deserve a proper investigation and treatment. Also after an episode of deep venous thrombosis it is now well demonstrated that treatment with medical elastic compression stockings will diminish the post-thrombotic symptoms by 50%.¹² However, not all patients need these stockings for the rest of their life and a proper test is needed to differentiate between the two groups. So, non-invasive techniques that are easy to perform, pleasant for the patient, economical and which have a good accuracy and reproducibility are strongly needed nowadays in phlebology.

A new promising test is the supine venous pump function test. With this test it is possible to evaluate the function of the deep veins of the lower extremities in a simple, accurate and patient friendly way. The test is performed with the use of SGP with the sensing gauge placed around the ankle (as described by van Gerwen).⁷ By performing ankle movements during an artificial venous hypertension, volume changes at the ankle are recorded and transformed into pressure changes by using an individual volume-pressure relation. The supine venous pump function test has been shown to be well correlated to direct venous pressure measurements.¹⁰

Air-plethysmography measures volume changes of the complete calf and not only of a segment as with strain-gauge plethysmography, so it could be expected to be more sensitive to use this technique in venous insufficiency. The APG is an established technique and has also been well correlated to ambulatory venous pressure measurements.

However, the results of this study clearly show that the APG method is not suitable in the supine venous pump function test, simply because it cannot discriminate between healthy and venous disease. Several explanations can be put forward. Firstly, the pressure in the venous system decreases from ankle to the heart under the influence of gravity. So, the venous pressure in the calf is lower than in the ankle. After performing exercises with the venous muscle pump the venous pressure will change (decrease). Differences between passive and active muscle movement are much more difficult to measure in the calf because the venous pressure in the calf is already much lower than at the ankle.

Secondly, the cuff of the APG measures the major part of the lower limb from ankle to knee. This is an advantage in the assessment of volume changes of the whole lower leg. However, for the supine venous pump function test it is not. The pressure data are derived from volume changes of the whole lower leg and not of a specific segment. The pressure data, derived from these measurements, will therefore become scattered. Furthermore it is unclear which part of volume changes measured with APG can be explained by changes of the venous volume and which part by volume changes of the muscle tissue.

A third important difference between the measurements performed by van Gerwen et al. is that they measured the venous footpump by placing the mercury-in-rubber strain gauges at 5-10 centimeter from the ankle. The APG cuff was placed around the whole lower leg, from ankle to knee and therefore we measured the pump function of the foot and calf. In the first method one compartment was measured, whereas in the second one deals with four or five

compartments of the calf. It is impossible to differentiate between them.

Finally it is difficult to perform APG measurements as has been argued by our group before.¹³ The investigated subject needs a good training to perform the investigation properly. We think that APG can be used to study volume changes of the leg and the effect of compression therapy on this without the patient having to move the limb.^{14,15} The movements of the patient is the most questionable handling in the APG measurements.

We conclude that APG is not suitable for supine venous pump function tests. Further studies are needed to establish whether the venous pump function test of the whole calf can be determined in a supine manner.

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CHAPTER 10

GENERAL DISCUSSION

Compression therapy is world wide accepted and practiced by many physicians treating patients with all kinds of phlebological diseases. Furthermore it is being used in patients with lymphoedema and some dermatological diseases such as erythema nodosum and vasculitis.¹ Surgical repair of the venous valves is still not possible in patients with deep venous reflux. If we only look at patients with a venous leg ulcer, more than 50% has reflux in the deep veins. All these patients will be assigned to compression therapy to prevent them from having complications such as dermato-et liposclerosis and ulceration. Many patients furthermore have a contra-indication for an operation or simply do not want an operation. Since the total incidence of leg ulcers is between 0.5 and 1%, it gives a good indication of the importance of the therapy. Compression is a cheap and effective treatment for this socio-economic burden called chronic venous insufficiency (CVI).² Another established indication for compression therapy by the use of compression stockings is thrombosis prophylaxis in combination with anticoagulants. In this case, elastic stockings with a pressure of less than 25 mmHg are normally being used.

Although compression therapy has already been used for hundreds of years, structural and fundamental research to the evidence of the treatment modality has only just begun. Before this time, bandages and stockings were only used because doctors knew empirically that they could improve the complaints of the patients. Different techniques for compression therapy are available for the treatment of venous diseases and disorders of the lymphatic system. The main forms are bandages, elastic compression stockings and mechanical pneumatic compression devices. Many beneficial effects of compression therapy have been demonstrated during the last 10 to 20 years. The majority of these studies have been performed in Germany, Austria, the Netherlands, Scandinavia and Great-Britain. The most important positive effects of compression therapy found in these studies were: increase in flow in the superficial as well as the deep veins, improvement of expelled volume, improvement of the calf muscle pump function and restoration of the shortened venous refilling time after exercise.^{3,4} Furthermore several different microcirculatory parameters return to normal after applying a bandage or wearing an elastic compression stocking. The abnormalities of the microcirculation play an important role in the development of the cutaneous complications which have been mentioned earlier in this chapter.

That compression therapy is of importance for many patients with CVI and other diseases such as lymphoedema, is unquestionable. However, several different aspects concerning practical topics and effectiveness of compression therapy are still unsolved or have never been investigated properly. Subjects such as working and resting pressure, stiffness factor and durability of elastic stockings are important in dailly practice for every phlebologist, dermatologist, surgeon, physician and general practitioner. However, the use of compression therapy is in major part not based on scientific evidence. Even guidelines for prescribing elastic compression stockings are only partly based on scientific research.⁵ So, this is a good justification for the study we have performed. It was the aim of this thesis to study clinical aspects of compression therapy. We have focused on those aspects which are especially useful for daily practice, such as which type of elastic stocking can be used in patients with

CVI, how much pressure should this stocking give at the ankle and what is its durability? Which type of bandage is most effective in patients with oedema and a venous leg ulcer? In this general discussion some of the results will be incorporated into practical advices for physicians treating patients with venous diseases or who are interested in compression therapy. At the end, we will discuss the results from the study in which we performed the supine venous pump function tests with air-plethysmography.

ELASTIC COMPRESSION STOCKINGS

Many patients daily use elastic compression stockings to prevent venous complaints and symptoms, such as oedema, dermato-et liposclerosis and ulceration. The Comité Européen de Normalisation (CEN) has made 4 different compression classes, each with a different indication area (see chapter 2). Compression class II elastic stockings are world wide the most frequently prescribed medical devices for phlebological diseases. The majority of patients using elastic stockings never have a proper follow-up or control of their symptoms and treatment.

Compression class

We measured the effect of different types of elastic compression stockings on the oedema prevention. Oedema is normally the first clinical sign of a decompensating venous system. The study was performed with air-plethysmography (APG). This technique is comparable with strain-gauge plethysmography, but has the great advantage that whole limb volume changes can be measured instead of small segments. Although relatively unknown in the Netherlands it is at this moment widely used, especially in the United States. With this technique we were able to demonstrate that antiembolism stockings and compression class I stockings (<25mmHg) have no value at all in the prevention of oedema. Because of this, a rationale for prescribing these stockings to phlebological patients, certainly in daily upright position, is lacking. Class II (25-35 mmHg) and III (35-45 mmHg) indeed demonstrated an oedema preventive effect. So these stockings should be used in all patients who suffer from having oedema at the ankle, or lower leg. It was interesting to measure a difference between round-knitted and flat-knitted stockings. The round-knitted stockings showed a better oedema protection. This is probably due to the used knitting materials. Another reason might be the stiffness factor or slope value, defined as increase in pressure (mmHg) of the stocking, when the circumference of the leg increases with 1 centimeter. This interesting aspect of the elastic compression stocking is relatively new, still hardly understood and a challenge for the near future.

The medial side at the ankle is the most important area for the phlebologist. More than 80% of all (venous) ulcerations of the leg occur at this place. So the effect of the compression should there be the highest. However, the anatomy of this part of the human body is unsuitable for an effective compression therapy. The surface is flat, so the pressure will be lower,

according to Laplace's law*. We were able to demonstrate that a compression class II stocking has a pressure at the medial site of only 74% of the mean pressure, measured around the ankle. So, when prescribing a compression class II stocking the physicians should realize that the majority of these medical devices will have a pressure of less than 25 mmHg at the medial B level, which is insufficient, and hence the treatment is not functional. This might be one of the reasons for the high recurrence rate of ulceration in patients who do wear their elastic therapeutic stockings in the correct way. We therefore advise to use compression class III stockings in all patients who have had a venous leg ulcer, and furthermore in all patients with severe venous symptoms. In this way, one is sure to have enough pressure at the medial side.

Pressure

The effect of an elastic compression stocking depends mainly on three factors: the pressure, the pressure gradient, and the stiffness factor. We measured the pressure underneath different types of elastic compression stockings. We could demonstrate in chapter 4 that all evaluated compression class II and III stockings produced sufficient pressure (especially class III), and a good pressure gradient proximal to the B1 level. From daily practice we have the impression that flat-knitted stockings normally show a better pressure gradient than round-knitted stockings, although we cannot substantiate this idea at the moment from the results. The continuous pressures measured at the dorsal foot, pretibial zone, and Achilles tendon were often more than 50 mmHg. So one has to be careful with patients having venous as well as arterial disease. These patients need specific individual attention, because serious side effects can occur. Unfortunately too many patients have been reported to have serious side effects due to improperly used stockings but also bandages. These side effects range from complaints of pain and superficial blistering to amputation due to necrosis.⁶

It is for all physicians working with elastic compression stockings good to realize that the pressure given by the manufacturer of the stockings will not be reached in a substantial part of the stockings. Nearly 1/4 (21.4%) of the compression class II stockings, measured in the study of chapter 6, were found to be insufficient (< 25 mmHg) at the time the patient started to wear them. Also the results from chapter 5 demonstrate that the mean pressure measured around the ankle in perfectly new and good fitting compression class II elastic stockings was 24.7 mmHg in supine, and 26.7 mmHg in standing position. So, also in this study there must have been quite a lot of (new) stockings with a pressure less than 25 mmHg. This lack of sufficient pressure at the moment the patient starts to wear the stocking seems to be a constant observation, and should be taken into account when the complaints of a patient do not improve.

We furthermore measured the pressure in one of the deep veins of the lower leg while wearing different types of elastic compression stockings (chapter 8). Although the number of measurements is small (n=8), we can conclude from the study that in supine, quiet lying position the mean pressure in the deep venous system only shows a clinical relevant increase

(75%) underneath strong compression class III elastic stockings with an ankle pressure of more than 40 mmHg. All other stockings showed a much smaller mean pressure rise (20-40%). Even the antiembolism stockings did produce a small increase (20%), supporting their activity in the prevention of deep vein thrombosis. In quiet standing position the pressure measured underneath all elastic stockings was equal and did not differ from the pressure measured without a stocking. This could be explained by the so-called hydrostatic paradox, which means that the pressure is equal irrespective the diameter of the vein. Unfortunately we were not able to measure the pressure in the deep veins during walking.

Durability

Recurrence of the complaints or ulceration is in most occasions the reason for patients to visit their doctor again. Replacement of elastic compression stockings have so far been performed on an empirical basis. In the Netherlands and also in other countries of the European community, patients get a prescription for medical elastic compression stockings twice a year, so in principle every six months. From the results of the durability study presented in chapter 6, we now know that the mean pressure of flat knitted as well as round-knitted stockings of compression class II is less than 25 mmHg at the ankle after 4 to 5 months. This pressure is generally accepted to be necessary to prevent patients from having oedema or worsening of skin symptoms in relation with CVI. The results of this study furthermore revealed that after 6 months about 2/3 of these compression class II stockings will have a pressure of less than 25 mmHg. We are convinced that this figure is unacceptable high. During the last two months before a patient receives a new stocking, more than half the patients use a stocking which is insufficient. It increases the risk of new ulceration with all problems and suffering for the patient, as well as the health costs. So, on the basis of the results from our durability study, we advise replacement of compression class II stockings three times a year instead of two. It is the absolute minimum to ensure efficacy of the treatment. This will eventually also be cost effective. Patients will have less complications, so their hospital visits will decrease. Class III flat knitted stockings performed better in our durability test. About 45% these stockings still showed a sufficient pressure (> 35 mmHg) at 6 months.

BANDAGES: ELASTIC OR NON ELASTIC?

The discussion on what kind of bandages to use for the treatment of phlebological complaints continues to exist. Many doctors treat their patients with specific bandages or elastic stockings, because they are used to, claim to have good results with them, have been trained to do so by their teachers, or have been influenced by the industry who spent a lot of money on advertising. However, hard evidence on the subject is scanty. Many studies lack power or have a bad design. It is however difficult to perform a proper study. This is mainly due to the fact that patients with venous complaints, such as ulceration, are often old and unwill-

ling to participate. The studies often show a high percentage of dropouts. Furthermore the tools for the investigations are often difficult to find or lack accuracy. We used the Oxford Pressure Monitor MKII because it is the best available interface pressure monitor at this moment. It has a good accuracy and reproducibility, is handy to use and inexpensive.

We could demonstrate that the pressure at the skin (so-called interface pressure) underneath short stretch bandages quite rapidly drops, after they have been applied (chapter 7). It is still 54% of the original pressure after 3 hours, and 37% after 7 days. Elastic bandages continue to give about the same amount of pressure after 3 hours. This is in complete accordance with studies performed by Callam and Travers, whose studies only differ in the time periods of measurements, and used materials.^{7,8} In a second part of the study we demonstrated that during walking short-stretch bandages have a 7% higher maximum pressure. The amplitude (maximum minus minimum) of the measured pressure during walking is twice as high as the elastic bandage. Just like underneath the elastic compression stocking, we found high pressures underneath both bandages on the dorsal foot, Achilles tendon and the pretibial area. We therefore advise that compression bandages should only be applied by trained people.

PELOTTES

A pelotte is a small piece of rubber used to increase local pressure over insufficient local perforating veins, but also to take away increased local pressure by correcting awkwardly shaped legs.⁹ Although very simple, it is an essential tool (in phlebology). We have demonstrated that the pressure exerted by both types bandages at the B-level is lower than the B1-level. The same was true for all types of elastic stockings. According to Laplace's law, the ankle anatomy has serious implications for the pressure exerted by a bandage or elastic compression stocking on the skin. The flatter the surface (like just above the medial malleolus) the bigger the radius and therefore the smaller the pressure on the skin will be. So compression treatment with bandages as well as elastic compression stockings should be combined with the use of pelottes, certainly if there is a substantial retromalleolar space. By this the shape of the leg will become more round and, in theory, the local pressure of the elastic stocking increases.

AIR PLETHYSMOGRAPHY

The last chapter of this thesis (chapter 9) on supine venous pump function test with air plethysmography may seem a bit strange since no compression therapy is involved. We have, however, two reasons for this incorporation. First, we believe that air-plethysmography is underestimated in the Netherlands. At this moment our department is the only one performing these measurements in the Netherlands! It is a functional test evaluating the

venous filling index (VFI) of the lower leg. This index has a high correlation with venous diseases and venous ulceration. At this moment there is a strong growing interest of surgeons and dermatologists in especially the United States for this type of investigation, and we believe this is correct. Other parameters measured with the APG have probably less sensitivity and specificity and should be interpreted with caution.

The second reason why we have taken this particular study as part of the thesis is because the recent thesis of van Gerwen in 1994 dealt with the subject of supine venous pumping test.¹⁰ So our study is a nice follow up. Van Gerwen et al. measured with strain-gauge plethysmography and found a good correlation with venous abnormalities and foot vein pressure measurements. We believe this supine venous function test is of great importance for the daily practice. It is therefore sad that in our comparative study using the APG, we could not reproduce their results. The main reason for this is the fact that there is a pressure gradient in the venous system along the lower limb. APG measures the complete volume of the lower limb and is therefore not suitable for this type of investigation.

SYNTHESIS

Compression therapy is essential in more than 50% of the patients with CVI and venous leg ulceration. In the active phase of the treatment oedema has to be reduced and the ulceration has to be healed. For the first ideally intermittent compression devices need to be used. As an alternative, elastic bandages can be applied for a short period of time, or non-elastic materials, if replaced as soon as the bandage starts to come down due to oedema reduction. When the oedema has disappeared and healing of the ulceration is the aim, non-elastic or short-stretch bandages are the best since they are more effective, safer and costs effective. We normally replace bandages in the beginning twice a week. Because the pressure decreases in time, especially when lying down, it will insure a proper arterial influx while the patient is sleeping or lying down. So these non-elastic bandages can stay on at night which is an important economical aspect. As soon as the ulcer has healed the maintenance phase starts. In this phase the treatment of choice is elastic compression stockings. For superficial venous insufficiency, stockings with an ankle pressure between 25 and 35 mmHg should be used and for deep venous insufficiency stocking with a pressure of at least 40 mmHg. In patients with awkwardly shaped legs due long longstanding CVI pads or pelottes should furthermore be used.

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SUMMARY

Chronic venous insufficiency (CVI) is a frequently occurring complex of symptoms caused by a continuous ambulatory venous hypertension. A disturbed lowering of the pressure in the superficial and deep venous system during walking plays a crucial role in this syndrome. CVI is caused by insufficiency of the superficial, perforating and/or deep venous system. Most common reason for venous insufficiency is primary varicosity or destruction of the venous valves after a deep venous thrombosis. Cornerstone in the treatment of CVI is compression therapy, either by elastic compression stockings or by compression bandages. Reviewing the literature on compression therapy, there is hardly any evidence on the beneficial effects of this form of treatment in patients with CVI. Therefore, up to now patients are being treated on an empirical basis. Simple measurements for the efficacy of the treatment in daily practice are not available, so the presence or absence oedema is normally taken to evaluate the effect of compression therapy. It was the aim of this thesis to get more insight into some pathophysiological and clinical aspects of compression therapy by means of compression bandages and elastic compression stockings.

In **chapter 1** a general review is given on venous insufficiency, varicose veins and venous ulceration. Particular attention has been paid to the history, anatomy and pathophysiology of the human venous system of the lower leg and to the epidemiology of venous diseases. This chapter also deals with some of the techniques available to diagnose venous disease.

In **chapter 2** a review is given on compression therapy. Compression therapy causes a reduction of oedema and an improvement of the ulcer healing process. The recurrence rate of venous ulceration is reduced. Further indications for positive effects of compression therapy are: correction of the elevated ambulatory venous pressure, improvement of the venous muscle pump function, increase of flow in the veins of the superficial as well as deep venous system, and finally improvement of the microcirculation of the skin in CVI, as measured by transcutaneous oxygen pressure and laser-Doppler.

In **chapter 3** the aims of the study are given. First it was the purpose to measure the effect of different types of elastic compression stockings on oedema prevention, and to measure the interface-pressure and pressure in the deep veins underneath these stockings. Furthermore it was our intention to evaluate the durability of elastic compression stockings. Another aim was to examine what type of bandages (elastic or non-elastic) should be used in the treatment of CVI. Finally, we were interested if air-plethysmography can be used to perform a recent introduced technique for the measurement of the venous pump function in supine position. In the second part of chapter 3 a justification is given of the patients which participated in the study, and the materials and techniques: Elastic stockings, Oxford Pressure Monitor, Air-plethysmograph, TNO-tester and deep venous pressure measurements.

In **chapter 4** the results are presented of a study measuring the interface pressure of elastic compression stockings in the first part, and the oedema preventive effects of these stockings in the second part. In the first part we used the Oxford Pressure Monitor MK II (OPM). With this technique it is possible to measure the pressure at 12 places underneath an elastic compression stocking. The results show a strong correlation between the compression class of the stocking and the pressure measured at the skin. All stockings showed a good pressure gradient from the B1 level upwards. The pressure at the B level was in all cases lower than the B1 level. This is caused by the elliptical shape of the ankle and the retromalleolar space. The results argue for the use of so-called pelottes or pads. The pressures measured at the Achilles tendon, dorsal foot and pretibial zone were sometimes extremely high. So attention should be paid in patients with complicated peripheral arterial disease. In the second part of the study the Air-plethysmograph (APG) was used. A cuff with a pressure of 70 mmHg was put on the upper leg. The increase in volume was measured before and during wearing 5 different elastic compression stockings. The results show a strong correlation between the compression class and the oedema prevention.

Chapter 5 deals with the results of a study which tries to explain the high recurrence rates of venous leg ulcers, even in patients who use their stockings properly. In this study a mathematical formula has been assumed, called Laplace's law: pressure equals the tension divided by the radius of the surface of the underlying leg segment. For the human leg this means that the pressure measured underneath the same elastic compression stocking will be less at the medial ankle than at the pretibial zone. Measurements were taken on 50 patients wearing new compression class II stockings. Using the OPM the pressure at 6 different places around the B-level (smallest circumference of the ankle) was determined. The results show that the mean pressure (24.7 mmHg) is just below the threshold of compression class II stockings (25 mmHg). The pressure at the medial site of the ankle (18.3 mmHg) is 26% below the mean pressure measured around the leg. At the pretibial zone the pressure (33.9 mmHg) is 36% higher. These results argue for the use of higher compression class stockings to reach sufficient pressure at the medial site (most frequent localization of venous ulcers). Also so-called pelottes can be used to increase locally the tissue pressure and thus the transmural pressure, resulting in localized oedema prevention. Theoretically this improves the venous refilling time and decreases the risk of ulcer recurrences.

In **chapter 6** the results of a durability test of elastic compression stockings are presented. So far no data are available about how long stockings continue to exert sufficient pressure. At this moment patients in the Netherlands receive a prescription every 6 months for new stockings. In this prospective study we measured 99 elastic compression stockings from 56 patients. Measurements were performed at the moment the patient started to wear the stocking, after 1 month and after 3 months. We used in this study the so-called TNO-tester. It is an official technique for pressure measurements of stockings. The results of the study show that compression class II stockings (flat as well as round-knitted) reach the critical pressure level of 25 mmHg between 4 and 5 months. At the start, already 21.4% of the stockings had

insufficient pressure (<25 mmHg). Individual regression-analysis revealed that after 6 months 66% of the tested compression class II stockings do not meet the critical pressure level anymore. If a 10% reliability margin is taken to ensure efficacy of the compression treatment, after 6 month 84% have past the threshold. Compression class III stockings performed better. On average they reach the critical pressure level of 35 mmHg after 6 months. Individual regression-analysis of these stockings showed that respectively 45% and 63% (without and with a 10% reliability margin) do not perform enough pressure after 6 months. On the basis of these results we recommend to replace compression class II stockings after 4 month, and III after 6 months. At the end this will be cost effectively since it has been well demonstrated that continuous adequate pressure reduces the risk of ulcer recurrence.

Chapter 7 deals with the results of a study in which we investigated what kind of compression bandages can best be used in the treatment of venous diseases. Using the Oxford Pressure Monitor the interface pressure was measured underneath a short-stretch and an elastic bandage. The study was performed on 39 legs of 35 subjects. Measurements took place immediately after the application of the bandage, after 1, and 3 hours and after 1, 3 and 7 days. The interface pressure measured underneath a short-stretch bandages decreased after 3 hours to 54% of the original pressure. After 7 days about 37% of pressure was left. Elastic bandages do not diminish in pressure at all after 1, and 3 hours.

In the second part we measured the interface pressure underneath short-stretch and elastic bandages while the test person walked on a treadmill at 4 km/hour. A total of 15 legs of 11 healthy volunteers were evaluated. The mean pressure during walking was equal underneath both bandages (short-stretch: 69.0 mmHg; elastic 70.1 mmHg). The working (maximal) pressure underneath the short-stretch bandage was significantly higher than underneath the elastic bandages (respectively 82.3 and 76.9 mmHg). Also the amplitude of the pressure (maximal minus minimal) is significantly higher in the short-stretch measurements (respectively: 29.2 and 13.6 mmHg). The results demonstrate that the use of short stretch bandages is not only safer but also more effective.

In **chapter 8** the influence of elastic compression stockings on the pressure in the deep venous system was evaluated with invasive pressure measurements. The study was performed on 8 legs of 7 volunteers (5 patients with CVI and 2 healthy volunteers). Via the popliteal vein a catheter was placed in one of the deep veins of the lower leg. By means of a pressure transducer the pressure was determined. Measurements were taken before and after the application of 5 different compression stockings (compression class I-III). The measurements were performed in the lying and standing position. The results show that in the lying position only stockings with a pressure of at least 40 mmHg at the ankle produce a clinical significant pressure increase in the deep veins of the lower leg. This suggests that only these stockings play a relevant role in deep venous pathology. So in patients with reflux in the deep veins of the lower legs, such as after a deep venous thrombosis, only stockings with an ankle pressure of 40 mmHg should be prescribed.

In **chapter 9** the results are given of a modified supine venous pump function test. In our setting we used the Air-plethysmograph (APG) for the determination of the venous pressure in the deep venous system in lying position. The major advantage of the APG compared to the strain-gauge plethysmograph (SGP), normally used for the supine venous pump function test, is that the APG measures volume differences of the whole lower leg whereas the SGP only a segment. The modification was tested on healthy subjects, patients with varicose veins and patients with a healed venous ulcer. The results showed a major overlap between healthy subjects and patients. There was no statistically significant difference between the 3 groups. So with the use of APG it is not possible to measure the venous pump function in supine position.

Chapter 10 contains a general discussion and a synthesis.

Based on the results reported in this thesis the following conclusions can be drawn:

- The pressure at the B level underneath elastic compression stockings as well as underneath compression bandages is in all cases lower than the B1 level, which is in contrast to the desired pressure gradient. Theoretically this can be solved in daily practice by the use of so-called pelottes.
- Short-stretch bandages are safer in the treatment of patients with CVI and have a better working and resting pressure relationship.
- Compression class I or antiembolism stockings no function concerning the prevention of oedema in patients with CVI.
- In the treatment of patients with deep venous insufficiency elastic stockings with at least 40 mmHg at the ankle should be used.
- The pressure of new compression class II stockings is in 21% of cases below the threshold (25 mmHg) of its compression class.
- Compression class II stockings have lost too much pressure after 4 months to be of clinical relevance anymore. For compression class III stockings this is after 6 months. So compression class II stockings have to be replaced three times a year and compression class III stockings two times.
- Airplethysmography is not suitable to measure the venous pump function in supine position.

SAMENVATTING

Chronisch veneuze insufficiëntie (CVI) is een vaak optredend symptomencomplex veroorzaakt door een continue ambulatoire veneuze hypertensie, waarbij een te geringe drukdaling in het veneuze stelsel tijdens het lopen centraal staat. Dit treedt op als gevolg van insufficiëntie van het oppervlakkige, perforerende en/of diepe veneuze systeem. Meest voorkomende reden voor deze insufficiëntie zijn primaire varices of een klepbeschadiging na een doorgemaakte diepe veneuze trombose. Hoeksteen bij de behandeling van CVI is compressietherapie, hetzij door middel van compressieverbanden, hetzij door elastisch therapeutische compressiekousen. Bij bestudering van de literatuur van compressietherapie blijkt er nog weinig 'evidence' te bestaan voor de positieve effecten van deze therapie bij de behandeling van patiënten met CVI. Tot op heden is deze voornamelijk op empirie gestoelde behandeling bijzonder nuttig voor een grote groep patiënten. Omdat een directe test ter verificatie van de effectiviteit van compressietherapie ontbreekt, geldt de aan-of afwezigheid van oedeem als de klinische parameter. Doel van dit proefschrift was meer inzicht te verkrijgen in enkele pathofysiologische en klinische aspecten van compressietherapie door middel van compressieve verbanden en elastische kousen.

In **hoofdstuk 1** wordt een algemeen overzicht gegeven van veneuze insufficiëntie, varices en het *ulcus cruris venosum*. Hierbij wordt aandacht besteed aan de geschiedenis van de flebologie, de anatomie en pathofysiologie van het menselijke venenstelsel en de epidemiologische gegevens van veneuze aandoeningen. Daarnaast komen in dit inleidende hoofdstuk enkele onderzoeksmethoden aan de orde, welke worden gebruikt bij de diagnostiek van veneuze insufficiëntie.

In **hoofdstuk 2** wordt een zo volledig mogelijk overzicht gegeven van datgene wat reeds in het verleden is gepubliceerd over compressietherapie. Laatstgenoemde bewerkstelligt een sterke oedeemreductie, verbetering van de wondgenezing bij het *ulcus cruris* en verlaging van het recidiepercentage na een doorgemaakt *ulcus*. Andere belangrijke aanwijzingen voor een gunstige invloed van compressietherapie bij verschijnselen van CVI zijn: correctie van de gestoorde veneuze drukdaling tijdens lopen, verbetering van de kuitspierpompfunctie, verhoging van de flow in de venen van het oppervlakkige en diepe systeem en tenslotte verbetering van de microcirculatie, gemeten met behulp van transcutane zuurstofmeting en laser-Doppler fluxmetrie.

In **hoofdstuk 3** wordt het doel van het onderzoek beschreven. Allereerst wilden wij het effect meten van verschillende typen elastische kousen op de oedeempreventie, naast de druk gemeten direct op de huid onder de kous en in het diepe veneuze systeem. Een ander doel in deze studie was de duurzaamheid van elastische therapeutische kousen te meten. Nog een onderdeel was te onderzoeken welk type verband (elastisch of niet-elastisch) het best gebruikt kan worden bij de behandeling van CVI. Tenslotte wilden we onderzoeken of

luchtplethysmografie geschikt is om de veneuze pompfunctie test in liggende positie uit te voeren. In een tweede deel van hoofdstuk 3 wordt een uitleg gegeven van de patientengroepen welke deelnamen aan de diverse onderzoeken. Tevens worden hier de daarbij gebruikte materialen en methoden besproken: elastisch therapeutische kousen, Oxford Pressure Monitor, lucht-plethysmograaf, TNO-tester, en de diepe veneuze drukmetingen.

In **hoofdstuk 4** worden in het eerste deel de resultaten gepresenteerd van een studie naar de druk op de huid welke elastische kousen uitoefenen, en in het tweede deel de invloed van deze medische hulpmiddelen op de oedeemneiging bij patiënten met CVI. Voor het eerste deel van de studie werd gebruikt gemaakt van de Oxford Pressure Monitor MK II. Het is met dit instrument mogelijk om de druk te meten op twaalf verschillende plaatsen van het been onder een kous of een verband. De resultaten tonen een duidelijke correlatie tussen de compressieklasse van de kous en de gemeten druk op de huid. Ook was er een drukgradient aanwezig bij alle kousen vanaf B1. De druk op de B-maat was in alle gevallen lager dan de druk op de B1-maat, hetgeen te maken heeft met de ellipsvormige structuur van het been en de retromalleolaire holte. De resultaten pleiten daardoor voor het gebruik van pelottes. De drukken, gemeten op de Achillespees, dorsale zijde van de voet en pretibiaal, waren vaak extreem hoog. Voorzichtigheid is dus geboden bij patiënten met tevens aanwezige arteriële vaatproblemen. In het tweede deel van de studie werd gebruik gemaakt van de lucht-plethysmograaf-methode (Engels: Air plethysmography of APG). Een cuff met een druk van 70 mmHg werd om het bovenbeen aangebracht. Vervolgens werd de volumetoename voor en tijdens het dragen van elastische compressiekousen van verschillende drukwaarde onderzocht. De resultaten tonen een duidelijke correlatie aan tussen de sterkte van de kous en de oedeempreventie.

Hoofdstuk 5 geeft de resultaten weer van een onderzoek dat werd opgezet om een verklaring te vinden voor het hoge percentage recidieven van veneuze ulcera, ook daar waar patiënten trouw hun kousen dragen. In de studie werd uitgegaan van een natuurkundige formule, de wet van Laplace: "bij toename van de straal van het oppervlak van het been zal de druk afnemen bij gelijkblijvende trekkracht van het verband of de kous". Op het menselijk been betekent dit dat de druk, gemeten onder eenzelfde elastische kous ter plaatse van de mediale malleolus, lager zal zijn dan op de tibia. Bij 50 patiënten, welke onze polikliniek bezochten in verband met CVI en die een nieuwe compressieklasse II kous droegen, werd op 6 verschillende plaatsen rondom het B-gebied (de smalste enkelmaat) de druk onder de kous bepaald. De druk werd gemeten met de Oxford Pressure Monitor MK II. De resultaten tonen dat de gemiddelde druk, gemeten op 6 plaatsen rondom het been, van compressieklasse II kousen (24.7 mmHg) net onder de gedefinieerde ondergrens van compressieklasse II kousen ligt. De resultaten tonen verder aan dat de druk ter plaatse van de mediale malleolus (18.3 mmHg) 26% lager is dan de gemiddelde druk gemeten rondom het been (6 plaatsen). Pretibiaal werd een 36% hogere drukwaarde gemeten (33.9 mmHg). De resultaten pleiten daarom voor het gebruik van kousen uit een hogere compressieklasse ten einde voldoende druk op het veneuze stelsel te bewerkstelligen. Ook kunnen zogenaamde pelottes

worden gebruikt ter plaatse van de mediale zijde van het onderbeen (meest frequente lokalisatie van het veneuze ulcus) om zo lokaal de weefseldruk en dus de transmurale druk te verhogen, resulterend in een lokale oedeempreventie. Theoretisch verbetert dit ook de veneuze hervullingstijd en vermindert het de kans op recidiefvorming.

In **hoofdstuk 6** worden de resultaten van een duurzaamheidstest van elastische compressiekousen weergegeven. Tot op heden bestaan geen studies waarin onderzocht werd hoe lang een elastische kous effectief zijn werking blijft doen. Momenteel krijgt een patiënt in de praktijk elke 6 maanden vergoeding van de zorgverzekeraars voor een nieuwe elastische kous. In totaal werden 99 kousen van 56 patiënten in deze prospectieve studie betrokken. Er werden metingen uitgevoerd op het moment dat de patiënt de kous ging dragen, na 1 maand en na 3 maanden. De metingen werden uitgevoerd met een TNO tester. Het is een officieel door de CEN erkende techniek die in Nederland door TNO gebruikt wordt voor de jaarlijkse kwaliteitscontrole van alle medische kousen, welke op de markt beschikbaar zijn. De resultaten tonen dat compressieklasse II vlak- en rondbreikousen hun kritische grens van 25 mmHg passeren tussen de 4 en 5 maanden. Bij aanvang van het dragen voldeed al 21.4% van de compressiekousen niet aan deze kritische grens. Met een individuele regressieanalyse kon worden berekend dat na 6 maanden 66% van de kousen niet meer voldeed aan de normering. Indien een 10% betrouwbaarheidsmarge wordt ingebouwd om de effectiviteit van de behandeling met elastische compressiekousen te verbeteren, zal na 6 maanden 84% niet meer voldoen. Bij compressieklasse III kousen zijn de uitkomsten gunstiger. Gemiddeld bereiken deze kousen na 6 maanden de kritische grens van 35 mmHg. Individuele regressieanalyse toont dat respectievelijk 45% en 63% (zonder en met een 10% veiligheidsmarge) na 6 maanden onvoldoende effectief meer is (<35 mmHg). De resultaten pleiten voor vervanging na 4 maanden van compressieklasse II vlak- en rondbreikousen, en na 6 maanden van compressieklasse III kousen. Uiteindelijk zal dit kosten-effectief zijn omdat bewezen is dat kousen met een continue adequate druk een vermindering van het ulcusrecidief teweegbrengen.

In **hoofdstuk 7** worden de resultaten beschreven van een studie die onderzocht welke verbanden (elastisch of kort-rek) in de praktijk het best gebruikt kunnen worden bij de behandeling van CVI. De druk op de huid (interface druk) werd gemeten met de Oxford Pressure Monitor MKII. De studie werd uitgevoerd op 39 benen van 35 personen. De metingen vonden plaats direct na het aanleggen van het verband, en vervolgens na 1, en 3 uur, en na 1, 3 en 7 dagen. De druk gemeten onder een kort-rek verband daalt na 3 uur tot 54% van de uitgangswaarde. Na 7 dagen is nog 37% van de uitgangswaarde over. Elastische verbanden verliezen weinig of niets van hun (interface) druk tijdens het dragen. In het tweede deel van de studie werd de interface druk gemeten onder de beide verschillende verbanden tijdens lopen van de proefpersoon met een snelheid van 4 km/h op een loopband. Hierbij werden 15 benen van 11 gezonde vrijwilligers onderzocht. De gemiddelde druk onder beide bandages was vrijwel gelijk (kort-rek verband: 69.0 mmHg en elastisch verband: 70.1 mmHg). De arbeids-

of werkdruk onder een kort-rek compressieverband was wel significant hoger dan onder een elastisch verband (respectievelijk 82.3 en 76.8 mmHg). Ook de drukamplitude (verschil maximale en minimale drukwaarden onder het verband tijdens het lopen) is significant groter en dus beter bij een kort-rek verband (respectievelijk 29.2 en 13.6 mmHg). De resultaten tonen aan dat het gebruik van kort-rek verbanden niet alleen veiliger is, maar ook effectiever.

In **hoofdstuk 8** werd de invloed van verschillende elastische compressiekousen op de druk in het diepe veneuze systeem gemeten met behulp van directe invasieve drukmetingen. Het onderzoek werd uitgevoerd op 8 benen van 7 vrijwilligers (5 patiënten met CVI en 2 gezonde vrijwilligers). Via de vena poplitea werd een catheter ingebracht in een der diepe venen. Door middel van een drukmanometer werd de druk ter plaatse gemeten. Dit werd gedaan zonder compressietherapie en vervolgens na het aantrekken van 5 verschillende soorten kousen uit de 3 verschillende compressieklassen (I t/m III). De metingen werden uitgevoerd in liggende en staande positie. De resultaten tonen aan dat alleen elastisch therapeutische kousen met een hoge drukwaarde (> 40 mmHg op het enkel niveau) een significante en klinische relevante stijging van de druk geven. Dit suggereert dat alleen deze kousen een klinische relevantie hebben bij diepe veneuze pathologie. Bij patiënten met een doorgemaakte diepe veneuze trombose, gecompliceerd door blijvende klepbeschadiging van de diepe venen, dienen derhalve alleen kousen te worden voorgeschreven uit een hoge compressieklasse (minimaal 40 mmHg enkeldruk).

In **hoofdstuk 9** werd een modificatie van de horizontale veneuze drukmeting volgens van Gerwen en medewerkers getest. In onze setting werd gebruik gemaakt van de lucht-plethysmograaf (Engels: Air-plethysmograph of APG) voor de bepaling van de veneuze druk in het diepe systeem in liggende positie. Voordeel van de lucht-plethysmograaf boven strain-gauge plethysmografie is dat de lucht-plethysmograaf volume-verschillen van het gehele onderbeen meet en de strain-gauge slechts van een segment. De methode werd getest bij gezonde vrijwilligers, patiënten met varices en patiënten met een doorgemaakt ulcus cruris venosum. Er blijkt een forse overlap in resultaten tussen de gezonden- en patiënten groep. Statistisch was er geen significant verschil tussen de groepen onderling. Met behulp van de lucht-plethysmograaf lijkt het derhalve niet mogelijk een horizontale drukmeting uit te voeren zoals eerder door van Gerwen en medewerkers in de literatuur beschreven met behulp van kwik-rek plethysmografie.

Hoofdstuk 10 bevat een algemene beschouwing van de verschillende onderzoeken en geeft een synthesis.

Op grond van de in dit proefschrift beschreven resultaten kunnen de volgende conclusies worden getrokken:

- De druk op het B-niveau onder een elastische kous én onder een compressieverband is in alle gevallen lager dan de druk op het B1-niveau, dit in tegenstelling tot de gewenste

drukgradient. Theoretisch kan dit in de praktijk worden opgelost door met pelottes te werken.

- Kort-rek verbanden zijn veiliger in gebruik bij patienten met CVI én hebben een betere werk- en rustdrukverhouding.
- Compressieklasse I- of antitrombose-kousen hebben geen waarde bij de bestrijding van oedeem bij patienten met CVI.
- Bij de behandeling van patienten met diepe veneuze insufficiëntie moeten elastische kousen worden gebruikt met een druk van tenminste 40 mmHg op het B-niveau.
- De druk van nieuwe compressieklasse II kousen is in 21% van de gevallen onder de kritische grens (25 mmHg).
- Compressieklasse II kousen hebben na 4 maanden te veel druk verloren om nog langer effectief te zijn. Voor compressieklasse III kousen geldt dit na 6 maanden. Derhalve dienen compressieklasse II kousen 3 maal per jaar, en compressieklasse III 2 maal per jaar vervangen te worden.
- Lucht-plethysmografie kan niet worden gebruikt bij het uitvoeren van de veneuze kuitspierpompfunctietest in liggende positie.

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List of abbreviations

AES	anti-embolism stocking
APG	air-plethysmography
AVP	ambulatory venous pressure
CEAP	clinical, etiological, anatomical, pathophysiological classification
CEN	Commission Européen de Normalisation
CMR	continue morbiditeitsregistratie
CVI	chronic venous insufficiency
DIN	Deutsches Institut für Normung
D-PPG	digital-photoplethysmography
DVT	deep venous thrombosis
ELAM-1	endothelial leucocyte adhesion molecule-1
ITF	Institut Textile de France
ICAM-1	intercellular adhesion molecule-1
LDF	laser Doppler fluxmetry
LRR	light reflex rheography
MST	medical stocking tester
OPM	Oxford pressure monitor
PAI-1	plasminogen activator inhibitor-1
PPG	photoplethysmography
s.d.	standard deviation
SGP	strain-gauge plethysmography
SVP	standing venous pressure
TcPO ₂	transcutaneous oxygen pressure
TNO	Nederlandse Organisatie voor Toegepast natuurwetenschappelijk onderzoek
VAR	veno-arteriolar reflex
VCAM-1	vascular cellular adhesion molecule-1
VRT	venous refilling time
WVP	walking venous pressure

CURRICULUM VITAE

De schrijver van dit proefschrift werd geboren op 3 december 1962 in Nijmegen.

Het diploma gymnasium 8 werd behaald aan het Bischoppelijk College Schöndeln te Roermond in 1981. In datzelfde jaar werd aangevangen met de studie Geneeskunde aan de Rijksuniversiteit Utrecht. Het artsexamen werd behaald in november 1988. Daarna was hij gedurende 6 maanden House Officer Surgery in een ziekenhuis in Shouth Shields (Engeland). Vanaf juli 1989 is hij werkzaam op de afdeling dermatologie van het Academische Ziekenhuis te Maastricht. Eerst als AGNIO en vanaf november 1992 als AGIO. Na zijn registratie als specialist op 1 mei 1996 is hij werkzaam als stafid binnen dezelfde vakgroep.

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